PATIENT SAFETY AND QUALITY ISSUES IN END STAGE RENAL DISEASE TREATMENT

HEARING

BEFORE THE

COMMITTEE ON WAYS AND MEANS U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED NINTH CONGRESS

SECOND SESSION

DECEMBER 6, 2006

Serial No. 109–87

Printed for the use of the Committee on Ways and Means

U.S. GOVERNMENT PRINTING OFFICE

35–773 WASHINGTON : 2007

For sale by the Superintendent of Documents, U.S. Government Printing Office
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CONTENTS

PATIENT SAFETY AND QUALITY ISSUES IN END STAGE RENAL DISEASE TREATMENT

WEDNESDAY, DECEMBER 6, 2006

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON WAYS AND MEANS,
Washington, DC.

The Committee met, pursuant to notice, at 10:45 a.m., in Room 1100, Longworth House Office Building, Hon. William M. Thomas (Chairman of the Committee) presiding.

[The advisory announcing the hearing follows:]

ADVISORY

FROM THE COMMITTEE ON WAYS AND MEANS

FOR IMMEDIATE RELEASE
November 29, 2006
FC–27

CONTACT: (202) 225–1721

Thomas Announces Hearing on Patient Safety and Quality Issues in End Stage Renal Disease Treatment

Congressman Bill Thomas (R–CA), Chairman of the Committee on Ways and Means, today announced that the Committee will hold a hearing on safety and quality for Medicare beneficiaries with End Stage Renal Disease (ESRD). **The hearing will take place on Wednesday, December 6, 2006, in the main Committee hearing room, 1100 Longworth House Office Building, beginning at 10:30 a.m.**

In view of the limited time available to hear witnesses, oral testimony at this hearing will be from invited witnesses only. Witnesses will include experts on Medicare payment and treatment of beneficiaries with ESRD and government officials. However, any individual or organization not scheduled for an oral appearance may submit a written statement for consideration by the Committee and for inclusion in the printed record of the hearing.

BACKGROUND:

In 1972, Medicare began to cover treatment for patients with kidney failure, known as ESRD. Patients with kidney failure are typically treated with dialysis and are prescribed medication to address anemia, calcium and other deficiencies.

Between 1998 and 2003, ESRD treatment spending increased by almost 50 percent. In 2004, Medicare covered about 309,300 dialysis patients, nearly 93 percent of all such patients in the United States. According to U.S. Renal Data System (USRDS) and the Medicare Payment Advisory Commission (MedPAC), Medicare spends about $64,000 per year for each person on hemodialysis for all medical services.

In the last 10 years, mortality rates for ESRD patients have declined except for patients that have been receiving therapy for 5 or more years. During the same time period, however, hospitalizations for infections and cardiovascular complications are up 20 and 10 percent, respectively. To address these problems, the Centers for Medicare and Medicaid Services (CMS) has taken steps to improve quality and safety in ESRD facilities. For instance, in 2004, CMS developed a dialysis facility comparison website that contains service and quality information on all Medicare approved dialysis facilities.

However, significant problems remain with the quality of care for patients that receive dialysis for kidney failure as well as the payments for this population. Two recent studies have indicated two specific concerns:

1. **Patient safety.** USRDS data show that 40 percent of patients in the dialysis population that are being treated with an anemia drug have a red blood cell count above the Food and Drug Administration (FDA) recommended level. Moreover, half of the 40 percent have a level associated with the higher risk of cardiovascular events and mortality, according to a November 2006 study published in the *New England Journal of Medicine.*
2. **Inefficient and unnecessary Medicare spending.** A recent study from November 2006 in *Dialysis and Transplantation* found that the population with a red blood cell count above industry guidelines also has higher drug costs, specifically, $3,100 per patient per year more just on the anemia drug.

In March 2006, the MedPAC reported that dialysis facilities continue to lose money on the composite rate, which includes the costs of nursing services, equipment and supplies. However, the losses are partially recouped by Medicare payment for drugs at Average Sales Price plus 6 percent. The Commission reported that the Medicare Modernization Act of 2003 (P.L. 108–173) made Medicare's drug payments less profitable in total, but also reported that the financial incentive to use more drugs persist even under the revised payment policy.

In announcing the hearing, Chairman Thomas stated, "While we have made gains in improving the End Stage Renal Disease program, clearly we need to continue to explore what more can be done to improve patient safety and quality of care. Patient safety and efficient use of taxpayer dollars are critical. We should examine the increased dosage of these drugs and the possible detrimental health effects. I am also concerned that Medicare has not been a prudent purchaser in this arena, given its rapid growth in spending. ESRD providers do not receive an annual update which is why a permanent solution that provides payment stability is critical to end perverse incentives based on the utilization of drugs."

FOCUS OF THE HEARING:

In continuing the Committee's consideration of improving the quality of health care in the Medicare program, the hearing will focus on recent research on the Medicare payment for drugs used in treating ESRD patients, the quality and safety of the treatment for ESRD patients as well as oversight on the CMS operations related to ESRD.

DETAILS FOR SUBMISSION OF WRITTEN COMMENTS:

Please Note: Any person(s) and/or organization(s) wishing to submit for the hearing record must follow the appropriate link on the hearing page of the Committee website and complete the informational forms. From the Committee homepage, *http://waysandmeans.house.gov*, select "*109th Congress*" from the menu entitled, "*Hearing Archives*" (*http://waysandmeans.house.gov/Hearings.asp?congress=17*). Select the hearing for which you would like to submit, and click on the link entitled, "*Click here to provide a submission for the record*." Once you have followed the online instructions, completing all informational forms and clicking "submit" on the final page, an email will be sent to the address which you supply confirming your interest in providing a submission for the record. You ***MUST REPLY*** to the email and ***ATTACH*** your submission as a Word or WordPerfect document, in compliance with the formatting requirements listed below, by close of business Wednesday, December 20, 2006. **Finally**, please note that due to the change in House mail policy, the U.S. Capitol Police will refuse sealed-package deliveries to all House Office Buildings. For questions, or if you encounter technical problems, please call (202) 225–1721.

FORMATTING REQUIREMENTS:

The Committee relies on electronic submissions for printing the official hearing record. As always, submissions will be included in the record according to the discretion of the Committee. The Committee will not alter the content of your submission, but we reserve the right to format it according to our guidelines. Any submission provided to the Committee by a witness, any supplementary materials submitted for the printed record, and any written comments in response to a request for written comments must conform to the guidelines listed below. Any submission or supplementary item not in compliance with these guidelines will not be printed, but will be maintained in the Committee files for review and use by the Committee.

1. All submissions and supplementary materials must be provided in Word or WordPerfect format and MUST NOT exceed a total of 10 pages, including attachments. Witnesses and submitters are advised that the Committee relies on electronic submissions for printing the official hearing record.

2. Copies of whole documents submitted as exhibit material will not be accepted for printing. Instead, exhibit material should be referenced and quoted or paraphrased. All exhibit material not meeting these specifications will be maintained in the Committee files for review and use by the Committee.

3. All submissions must include a list of all clients, persons, and/or organizations on whose behalf the witness appears. A supplemental sheet must accompany each submission listing the name, company, address, telephone and fax numbers of each witness.

Note: All Committee advisories and news releases are available on the World Wide Web at *http://waysandmeans.house.gov*.

The Committee seeks to make its facilities accessible to persons with disabilities. If you are in need of special accommodations, please call 202–225–1721 or 202–226–3411 TTD/TTY in advance of the event (four business days notice is requested). Questions with regard to special accommodation needs in general (including availability of Committee materials in alternative formats) may be directed to the Committee as noted above.

Chairman THOMAS. Good morning. First of all, I want to thank our witnesses and the Members of the Committee. In an attempt to make sure that we can utilize the time as usefully as possible on a very important hearing—made more timely by recent publications that were released in a GAO study—notwithstanding the fact we are in a lame duck session in which system negotiations are occurring between the House and the Senate; therefore, we have asked the panel of specific experts who have a body of written information that has been available, and they will comment directly on that. The Chair would request that Members limit any questioning if at all possible, so that we could delve then relatively quickly to members of the administration of the GAO, who have time constraints of their own.

The Committee will hear from our distinguished panel of witnesses, basically, whether Medicare is appropriately safeguarding the packets and the integrity of the trust funds because, recently, the scientific and even mainstream press have pointed out a growing concern about unsafe and questionable treatment for Medicare's coverage for kidney failure, also known as End Stage Renal Disease.

We know that for more than 30 years Medicare has covered treatments for patients with ESRD. Treatments usually consist of dialysis, also with anemia, a lower number of red blood cells, drugs. Medicare payments for these treatments have increased rapidly by almost 50 percent between 1998 and 2003. In fact, one of the drugs to treat ESRD has been identified as the single largest expenditure in Medicare part B each year, notwithstanding the small population that receives the drug. More importantly, there has been longstanding safety concerns about whether patients receiving treatment for ESRD are actually being harmed by the perhaps high doses of anemia drugs they are prescribed. According to the U.S. Renal Data System 40 percent of the dialysis patients treated for low red blood cells with anemia drugs actually have a red blood cell count above the FDA recommended levels. In fact, after the drugs, beneficiaries have a level high enough to trigger serious cardiovascular problems, some resulting in death. So, the question is not only one of taxpayers' money being spent on a monopoly drug; it is the question of what is reasonable and appropriate from a health point of view.

We are also anxious to hear testimony from the Centers for Medicare and Medicaid Services, CMS. In April of this year, the Chair wrote to then administrator Mark McClellan asking several

pointed questions about why CMS had developed the policy to deal with what we considered to a certain extent out-of-control dosing of ESRD patients at a different level than the FDA recommended and the labels on the drugs prescribed.

If this was the right policy, the Chair believes it should have been easy to answer the letter. It took CMS 8 months, until this week in fact, to respond. Then, again, in November, not having that in a response, House Subcommittee Ranking Member Stark and the Chairman wrote a letter to Acting Administrator Norwalk—and the Committee appreciates her ability to attend today—reiterating our concerns. Again, the letter was not responded to until Monday night. Obviously, today we are going to talk about the letter response but, more importantly, the concerns that the letter reflected.

Now, after a number of months and having seen a significant number of publications focusing on exactly those issues, hopefully, we will be able to get some understanding of the issue of the treatment for patients. Obviously, we are going to solicit ideas for improving qualities for these beneficiaries, and we are interested in hearing now the GAO's testimony following the release yesterday of their report on Medicare payment for ESRD services. We have a significant document, a printed evidentiary record, that will be in front of us, and we want to know where we are going to go from here.

So I am excited about this hearing. Obviously, this is the beginning, notwithstanding the fact it is coming at the end of this Congress; these questions will obviously carryover. I appreciate the ongoing bipartisan working relationship that we have had on this very important issue, and I will recognize the gentleman from New York for any statement he may wish to make.

Mr. RANGEL. Thank you, Mr. Chairman. This meeting is historic for a variety of reasons. One, because you visited with us in the Democratic Caucus together and made it clear that you and Peter Stark were in agreement on this subject matter. For us, that is a gigantic step, and we wanted that to be properly recorded.

The second thing——

Chairman THOMAS. Would the gentleman yield?

Mr. RANGEL. I would be pleased.

Chairman THOMAS. I am pleased you finally got it right.

Mr. RANGEL. The second thing is this probably will be the last formal hearing that you will be chairing. I think the audience should know that, notwithstanding what the record would indicate, these Committee hearings, as it relates to your relationship with me, that the audience should know that Bill Thomas and I have never, but never, in the years that we have served in the House of Representatives had an unpleasant conversation outside of the Committee room.

I also would like to say that the Committee has agreed, and I have agreed, to host the reception that was supposed to be a surprise, but knowing how difficult it is in the last few days of our work, that we hope that you will be available at 5:00 tomorrow when the Committee members and staff would like to thank you for the dedication which you have given to the Committee, the Congress, and the country.

Lastly, we would like to wish you a happy birthday. This is your 65th birthday, and now I can see why you are concerned about Social Security, as you become eligible for Medicare, and I have personally had a special Social Security card made up in connection with reform that Jim McCrery and I are going to be working on, and I have signed this so that if you have any problems at all, you can rest assured that this will be able to get you the proper health care that you might need.

Chairman THOMAS. I want to thank the—this looks like the $3 bill he gave me last year. The gentleman needs to know that, unfortunately, I voted for the extension of age not nearly long enough based on life expectancy so I don't get to use my Social Security card until I am 65 years, 8 months. However, Medicare kicks in immediately and hence the reason for this particular hearing.

Mr. RANGEL. I would like to yield the substantive questions to your colleague, Peter Stark.

Mr. STARK. Thank you.

Thanks, Bill. My wishes for a happy 65th birthday. I wish I could remember what I did on mine.

But now that you are no longer just an observer, I want to ensure you that we will do our best to make it a successful program for you and all Americans.

I am pleased to call this hearing. It is—the ESRD policy is unique in our country. Some may say it is our only form of socialized medicine. Almost everybody who is involved in dialysis is involved in the government finance program. One of the problems that we have had is that we have been involved in using these drugs which have cost us a couple billion dollars a year, and many of us have maintained for a long time that we should be getting a better deal. We are now faced with the potential that we may actually, through policies of reimbursement, be putting people at risk for danger to their health, and that is something that I don't think we should tolerate.

I wanted as many of you in the room to know I have a long history on this issue, and it has come to my attention, Mr. Chairman, that recently certain interests may be misrepresenting my past positions, and I would just like to submit for the record a copy of a letter I wrote to CMS in 1997 that has been circulated and a written response from my then lead staff person Bill Vaughan who helped draft my response, and I just add this to clarify the record if Mr. Chairman would accept.

Chairman THOMAS. Without objection.

[The information follows:]

November 29, 2006

The Honorable Fortney H. (Pete) Stark
Ranking Member, Subcommittee on Health
Committee on Ways and Means
239 Cannon House Office Building

Dear Congressman Stark:

As a former staff member who served on the Ways and Means Health Subcommittee between 1996 and the spring of 2001, your current staff has asked me to elaborate on the letter you asked me to draft, and which you signed, addressed to former Health Care Financing Administrator Nancy-Ann DeParle dated December 8, 1997 relating to Medicare coverage of EPO.

Apparently someone—who has not read the letter thoroughly—is alleging that this letter indicates your support of higher dosages of EPO. That is a complete misreading of your letter. Your letter was an effort to encourage the removal of financial incentives that have long distorted the administration of EPO—a distortion that has cost taxpayers hundreds of millions—perhaps billions!—of dollars and which we now find may have been hurting the health of hundreds of thousands of patients. As you repeatedly stressed to me, your goal on the Subcommittee has always been to encourage the best practice of medicine, without financial influences to over—or under—treat patients. This letter is part of that theme—a theme seen in your other efforts, such as the physician referral laws (Stark I and II) and your successful amendment to limit the amount that managed care physicians can be financially placed at risk for under-treatment of patients.

Because historically there has been a spread between what Medicare reimburses a dialysis center for a unit of EPO and what the company's net selling cost of the product to the center is, centers have profited by increasing their use of EPO. I once even saw a chart that a salesperson for the company gave to dialysis clients showing how profit would increase as dosage was increased!

Only by eliminating the profit incentive to administer higher and higher doses can patients have the peace of mind that they are getting an appropriate level of EPO. Ideally, in my opinion, centers would be reimbursed for their net acquisition cost plus a dollar for administration (since it is generally administered through an existing line to the patient).

The VA, Kaiser, and most of Europe generally (but on a case by case basis) administers EPO subcutaneously, which in most people results in the more efficient uptake of the medicine and can save substantial amounts of money because less EPO is necessary to achieve the same hematocrits. I urge you to encourage such a policy, perhaps sharing the savings with beneficiaries through reduced copayments as compensation for the inconvenience of the injection. It would also be useful to ask if the company has finally made a dose formulation that minimizes any pain of injection.

The December 8, 1997 letter was written before I remember ever seeing any studies (such as those excellent papers by Dennis Cotter, et. al) raising safety concerns of over-dosage. It was written before the recent important discussion of CMS dosage rates exceeding FDA recommended dosages. In writing the letter, we were concerned that the HCFA policy would cause centers to under-dose because of fear of non-payment. Under-dosing for financial reasons is clearly as bad as over-dosing for financial gain. Your letter was designed to deal with both issues: allow upward dosing where a physician thought it was appropriate, but take away almost all of the overpayment incentive that was causing over-dosing for financial gain.

As a former staffer, who organized the very first Ways and Means oversight hearings on the ESRD program in 1975, I have long felt that the financial incentives in this program have been an abuse to the taxpayer and to the best care of patients. I deeply regret that we did not make more progress on this issue when I was one of your staff members, and I wish you the best in finally achieving good health policy at a reasonable cost to taxpayers.

Sincerely,

William Vaughan

P.S. Don't cap medical malpractice! Maybe it's time for someone to get sued for the abuse of patients in this sector.

Mr. STARK. I look forward to hearing from our witnesses.

Chairman THOMAS. Any other member may put a written statement in the record. Our witnesses have an extensive body of studies and the rest, and my goal would be to have you present in a very succinct way, in the time you have available, the key points you might want to make based upon these recent studies, which have obviously been very timely and focused us on the concerns that we had, some general concerns that clearly now have been evidenced by clinical studies as well. It seems to me, given the three panelists, that we would start with Dr. Pizzi for no other reason than the fact that you are in the middle.

STATEMENT OF LAURA T. PIZZI, PharmD, MPH, RESEARCH ASSOCIATE PROFESSOR OF HEALTH POLICY, DEPARTMENT OF HEALTH POLICY, THOMAS JEFFERSON UNIVERSITY, PHILADELPHIA, PENNSYLVANIA

Dr. PIZZI. Chairman Thomas and distinguished Committee members. My name is Dr. Laura Pizzi. I am research associate professor of health policy at Jefferson Medical College in Philadelphia. I am a pharmacist by training but for the past 10 years have worked as a researcher on issues related to the costs and outcomes of pharmaceuticals and presently lead a group of six researchers at Jefferson who are dedicated to this topic. I hold the secondary appointment as adjunct assistant professor in pharmaceutical business at the University of Sciences in Philadelphia and am co-editor of the text entitled, Economic Evaluation in U.S. Health Care, Principles and Applications, which was released last year.

I am here today to discuss the results of a study that I led at Jefferson which was published in the November 2006 journal, Dialysis and Transplantation. This study was conducted by our team at Jefferson along with Dr. David Goldfarb, who is a nephrologist at the New York Harbor Veterans Affairs Medical Center in New York City, and Dr. Joseph Fuhr, who is a professor of economics in Chester, Pennsylvania. The study was funded by a grant from Watson: Laboratories. While we received funding from Watson, our team formulated the research objective, designed the study, and performed the analysis independently. My testimony does not reflect the views of the sponsor nor of Jefferson.

The objective of this study was to determine the extent to which health care providers adhered to clinical practice guidelines for the treatment of anemia in patients receiving hemodialysis. The guidelines that we used were those published by the Kidney Disease Outcomes Qualified Initiative, also known as KDOQI, released in the year 2000 by the National Kidney Foundation. We compared actual utilization in practice for the anemia drugs, erythropoietin, or EPO, and intravenous iron to the KDOQI 2000 guideline recommendations. Actual utilization was obtained from the United States Renal Data Service annual report for 2004.

The critical target for anemia in this population was a hemoglobin of 11-12 mg/dL. To reach this hemoglobin level, patients need to have their iron stores replenished with intravenous iron, and they also need to receive EPO to stimulate red blood cell production. The guideline calls for an initial EPO of 120-180 units per kg per week, which we assumed remained the dose during the study period. We calculated recommended dosages based on the average weight of an adult receiving hemodialysis, 159.5 pounds.

For iron, we used recommended doses from KDOQI. We then examined actual utilization per the United States Renal Data Service Data and compared it to what was recommended by the KDOQI 2000 guidelines. Our findings indicated that there was significant overuse of EPO and slight underuse of intravenous iron. Although we were not surprised to see that the providers were not strictly adhering to the guideline, we were quite surprised by the extent to which EPO use in practice deviated from KDOQI recommendations.

Next, we converted the difference in utilization to dollars based on 2005 Medicare reimbursement rates. We estimate that CMS could have reduced expenditures for these drugs by 36 percent if dialysis facilities adhered to the guidelines. If CMS spends $2 billion per year on EPO, it is reasonable to say that several hundred million dollars could have been saved if the providers followed the guidelines.

Chairman THOMAS. Dr. Pizzi, you are down to about a minute, and I would prefer that you move to your recommendations and conclusions, because we have your written testimony, and it will be made a part of the record.

Dr. PIZZI. I believe the best way to address the matter of EPO overuse is to reward dialysis providers who achieve an appropriate hemoglobin target—whether the target is based on KDOQI recommendations, product labeling, expert opinion, or a combination of these sources. Once the target has been agreed upon, CMS may wish to consider a pay-for-performance reimbursement policy centered upon that hemoglobin target as follows: Lower the reimbursement rate for EPO such that it is cost neutral to the facilities and reward facilities with a higher reimbursement rate for the dialysis session for patients whose hemoglobin is in the target range.

In conclusion, the results of our study indicate that EPO use far exceeded what was recommended in the KDOQI guideline during the study period. Despite changes in the guideline as well as the Medicare reimbursement policy, I believe EPO is still being used in excess today.

I thank you very much for your consideration and hope that a pay-for-performance-based reimbursement policy will be evaluated as a means to ensure sufficient treatment for this vulnerable population.

Thank you very much.

[The prepared statement of Dr. Pizzi follows:]

Statement of Laura T. Pizzi, Research Associate Professor of Health Policy, Department of Health Policy, Thomas Jefferson University, Philadelphia, Pennsylvania

Chairman Thomas and distinguished Committee Members, my name is Dr. Laura Pizzi and I am a Research Associate Professor of Health Policy at Jefferson Medical College in Philadelphia. I am a pharmacist by training, but for the past 10 years have worked as a researcher on issues related to pharmaceutical cost and outcomes and presently lead a group of 6 researchers at Jefferson who are dedicated to this topic. I hold a secondary appointment as Adjunct Assistant Professor of Pharmaceutical Business at the University of the Sciences in Philadelphia and am co-editor of the text entitled "Economic Evaluation in U.S. Healthcare: Principles and Applications" which was released last year.

I am here today to discuss the results of a study that I led at Jefferson, which was published in the November 2006 issue of the journal *Dialysis and Transplantation.*[1] This study was conducted by our team at Jefferson, along with Dr. David Goldfarb who is a nephrologist at New York Harbor Department of Veterans Affairs Medical Center in New York City and Dr. Joseph Fuhr who is a professor of economics at Widener University in Chester, Pennsylvania.

The study was funded by a grant from Watson Laboratories in Morristown NJ. While we received funding from Watson, our team formulated the research objective, designed the study, and performed the analysis independently. My testimony does not reflect the views of the sponsor nor of Jefferson.

[1] Pizzi LT, Patel NM, Maio VM, Goldfarb DS, Michael B, Fuhr JP, and Goldfarb NI. Economic Implications of Non-adherence to Treatment Recommendations for Hemodialysis Patients with Anemia. *Dialysis and Transplantation* 2006;1–7.

Summary of the Study

The objective of this study was to determine the extent to which healthcare providers adhere to clinical practice guidelines for the treatment of anemia in patients receiving hemodialysis. The guidelines that we used were those published by the Kidney Disease Outcomes Quality Initiative (KDOQI), released in the year 2000 by the National Kidney Foundation.[2]

We compared actual utilization in practice for the anemia drugs, erythropoietin or "EPO" and intravenous iron to the KDOQI 2000 guideline recommendations. Actual utilization was obtained from the United States Renal Data Service (USRDS) Annual Report for 2004, which includes 431,284 active patients.[3] This data source captures patient and facility records from the CMS End Stage Renal Disease (ESRD) Program's Management and Medical Information System, an Annual Facility Survey, and data related to services delivered via Medicare, including treatments administered to ESRD patients, patient outcomes, and costs. The report is updated annually.

From USRDS, we obtained the total number of Medicare beneficiaries who received hemodialysis, which was 372,643. Approximately 96% received EPO at least once during a 3 month period.

The clinical target for treatment of anemia in this population, per the KDOQI 2000 recommendations, was a hemoglobin level of 11–12 mg/dL. To reach this hemoglobin level, patients need to have their iron stores replenished with intravenous iron, and they also need to receive EPO, which stimulates red blood cell production and thereby works to correct the anemia. The recommended target for iron stores was a serum ferritin level of at least 100ng/mL.

The guideline called for an initial EPO dose of 120–180 units per kg per week, which we assume remained the dose during the study period. We calculated the recommended dosage of EPO based on a 72.5 kg adult, which is the average weight of hemodialysis patients reported by USRDS. For iron, the recommended dose for adults was 100–125mg given intravenously at every hemodialysis session for 8–10 doses followed by a maintenance dose of 25–125mg per week upon reaching the target ferritin level.

We then examined actual utilization, per USRDS 2004, and compared it to what was recommended by the KDOQI 2000 guidelines. Our findings indicated that there was significant over use of EPO and slight under use of intravenous iron. Although we were not surprised to see that providers were not strictly adhering to the guideline, we were quite surprised by the extent to which EPO use in practice deviated from KDOQI recommendations.

Next, we converted the difference in utilization, which was actual versus recommended practice, to dollars based on 2005 Medicare reimbursement rates for EPO and iron. We estimate that CMS could have reduced expenditures for these drugs by 36% if dialysis facilities adhered to the guidelines. If CMS spends $2 billion per year on EPO, it is reasonable to say that several hundred million dollars could have been saved on the drug if providers followed the guidelines.

Recent Data

If we were to repeat our study today using the same clinical target but newer data from the 2006 USRDS Annual Report, our findings regarding EPO over use would hold, because the mean EPO dose according to this latest report is similar to what we used in our study. Specifically, the mean monthly EPO dose that we used in our study was 76,473 units per month, and data from 2006 USRDS shows a mean monthly EPO dose ranging from approximately 72,000–81,000 units per month in calendar year 2005.[4]

In addition to the costs resulting from EPO overuse, safety concerns have emerged about maintaining hemoglobin levels above 13.5mg/dL, as we know from Dr. Singh's testimony on the findings from the Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) trial.[5] In response to this study, the FDA issued an Alert on November 16, 2006, which states that the target hemoglobin for EPO

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[2] National Kidney Foundation. KDOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease 2000. *American Journal of Kidney Disease* 2000; 37:S182–S238 (suppl 1).

[3] USRDS Annual Data Report 2004. Available at: http://www.usrds.org/adr_2004.htm (Accessed 27 Nov 2006)

[4] USRDS Annual Data Report 2006. Table 5.37. Available at: http://www.usrds.org/atlas.htm (Accessed 29 Nov 2006)

[5] Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, and Reddan D, for the Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) Investigators. Correction of anemia with epoetin alfa in chronic kidney disease. *New England Journal of Medicine* 2006; 355:2085–98.

should not exceed 12 g/dL.[6] Although the KDOQI guidelines were recently updated in 2006 and now recommend a hemoglobin ≥11g/dL while not routinely maintaining the level ≥13g/dL, the upper threshold of 13g/dL was established prior to publication of the CHOIR. As a result of these developments, the National Kidney Foundation announced last week that it will convene an expert panel to assess EPO use.[7]

Hence, though our study focused on the *economic impact* of non-adherence to the guidelines, very recent data and concerns have emerged about the *safety impact* of maintaining a hemoglobin level exceeding 12g/dL. These recent events, coupled with the results from our study, provide evidence that it is time to more aggressively manage EPO use in dialysis facilities.

Recommendations

In the time since our study was completed, CMS did change the reimbursement policy for EPO. The revised payment policy required the dose to be reduced by 25% when the hemoglobin exceeded 13g/dL.[8, 9] Providers who failed to reduce the EPO dose by 25% received a payment reduced by 25%, unless the higher dose was approved through an appeals process. This policy change marked a step towards more efficient treatment, however in my opinion, it will not sufficiently stimulate renal dialysis facilities to achieve the clinical target.

I believe that the best way to address the matter of EPO over use is to reward dialysis providers who achieve an appropriate hemoglobin target—whether that target is based on the KDOQI recommendations, product labeling, expert opinion, or a combination of those sources. Clearly, a target hemoglobin of 11–12mg/dL is appropriate, but there is uncertainty about whether the window should be expanded to include hemoglobin levels between 12 and 13mg/dL. I trust that Dr. Singh's research along with the recommendations from the National Kidney Foundation's expert panel will help to inform this matter.

Once the target has been agreed upon, CMS may wish to consider a pay-for-performance reimbursement policy centered upon that hemoglobin target as follows:

1. Lower the reimbursement for EPO such that it is cost-neutral to the facility
2. Reward facilities with a higher reimbursement rate for the dialysis session (composite rate) for patients' whose hemoglobin is in the target range

CMS might also consider further boosting the composite rate for patients who are given subcutaneous EPO (as opposed to intravenous EPO), because administering the drug subcutaneously has been shown to require significantly lower dosages.[10, 11, 12, 13]

It is important to keep in mind, however, that pay-for-performance measures do not necessarily reduce costs, and an increase in the base composite rate may be necessary to maintain the supply of dialysis facilities. In other words, some amount of monies that would have otherwise been spent on EPO would be re-allocated to dialysis facilities through the composite rate. However, implementation of the policy would stimulate dialysis facilities to use EPO more efficiently and would reduce their reliance on revenues from the product.

Conclusion

In conclusion, the results of our study indicate that EPO use far exceeded what was recommended in the KDOQI guideline during the study period. Despite changes in the guideline as well as the Medicare reimbursement policy, I believe that EPO

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[6] Information for Healthcare Professionals: Erythropoiesis Stimulating Agents (ESA) [Aranesp (darbepoetin), Epogen (epoetin alfa), and Procrit (epoetin alfa)]. FDA ALERT 11/16/2006. Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/RHE_HCP.pdf (Accessed 27 Nov 2006)

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is still used in excess today, primarily because dialysis facilities do not have a financial incentive to manage its use. Thank you very much for your consideration and I hope that a pay-for-performance based reimbursement policy for EPO will be evaluated as a means of ensuring the safe and efficient treatment of anemia in this vulnerable population.

Chairman THOMAS. Thank you. I apologize moving you to that, but the statement that you have made is based upon data that is well known and published.

Dr. Singh.

STATEMENT OF AJAY K. SINGH, MBBS, MRCP (UK), MBA, CLINICAL CHIEF, RENAL DIVISION, DIRECTOR, DIALYSIS SERVICES, BRIGHAM AND WOMEN'S HOSPITAL, HARVARD MEDICAL SCHOOL

Dr. SINGH. Chairman Thomas and distinguished Committee members. My name is Dr. Ajay Singh. I am the clinical chief of the Renal Division and director of dialysis Services and a physician at the Brigham and Women's Hospital and an associate professor of medicine at Harvard Medical School. I practice medicine, teach physicians and students, and conduct patient-oriented research. I am the first author and one of the principal investigators of the CHOIR study. My written remarks will be submitted as part of the record, and I wish to just focus on the top conclusions from the CHOIR study.

In the CHOIR study, we tested whether targeting a hemoglobin of 13.5 grams per deciliter versus a hemoglobin of 11.3 grams per deciliter in patients with chronic kidney disease not on dialysis was associated with a survival benefit and lower cardiovascular complications. To our surprise, patients who were randomized with the higher hemoglobin group had an excess risk of 34 percent with respect to death and cardiovascular complications compared to those patients randomized to the lower hemoglobin group.

Of note, we also found there were 52 deaths in the higher hemoglobin group versus 36 deaths in the lower hemoglobin group, a hazard ratio of 1.48 or a 48 percent higher risk. We also found a higher risk for hospitalization for heart failure to 41 percent higher risk. We did not find any incremental improvement in quality of life for three different parameters of quality of life that we tested, and we also found that for cardiovascular risk adverse events, there were more adverse events in the higher hemoglobin group versus the lower. Therefore, the conclusion was there was both increased risk and no substantive incremental quality of life benefit in raising the hemoglobin among patients with chronic kidney disease not on dialysis.

Now, some have argued that while this study looked at patients with chronic kidney disease not on dialysis and this data should not apply to patients on dialysis, I would respectfully disagree with that. Both the National Kidney Foundation guidelines, the European Best Practice guidelines of anemia as well as the FDA label have aggregated patients not on dialysis with kidney disease with those on dialysis and have framed guidelines with respect to the higher hemoglobin level. Until we get further data, I would argue that we should default in the direction of patient safety by aiming

for hemoglobin levels no higher than 12 grams per deciliter, and our recommendation of the paper was 11–12 grams a deciliter of hemoglobin.

The other aspect of this was the issue of what one should do with the rising number of proportional patients on dialysis that have hemoglobin levels beyond 12 grams per deciliter. As the Committee will note as part of the record information, there are a number—there are a number of dialysis providers who have patients who have hemoglobin levels above this 12-grams-per-deciliter-range. Based on this study and some other controlled studies, I would suggest and agree with the notion that we should adopt a bundling for epoetin because it confers with the potential of benefit without incentives, financial incentives, to use higher levels of epoetin or aim for higher hemoglobin levels. The only caveat I would suggest, there would be some form of risk assessment in the patient population so that providers are not disincentivized to treat sicker patients.

So, in conclusion, our study as well as studies that have been published prior to this suggest increased risk in raising the hemoglobin level beyond 12 grams. I believe that this will further reinforce the FDA label, which is clear, and a new alert was published recently. I believe that this recommendation should apply to both dialysis patients as well as pre-dialysis patients until we have more evidence from studies that hopefully will be funded in the future. I believe that the best recourse to try and prevent hemoglobin levels rising in both the dialysis population is to take the approach of bundling of services so that there is—we remove the financial incentives to use larger doses of EPO and aim for higher hemoglobin levels.

[The prepared statement of Dr. Singh follows:]

Statement of Ajay K. Singh, Associate Professor of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

I am Dr. Ajay K. Singh, Clinical Chief, Renal Division and Director, Dialysis Services and a physician at the Brigham and Women's Hospital and an Associate Professor of Medicine at Harvard Medical School. I practice medicine, teach physicians and students, and conduct patient-oriented research. I am the first author and one of the Principal Investigators of the CHOIR study. This study examined the effect of normalizing the hemoglobin with epoetin alfa in patients with chronic kidney disease not receiving dialysis. My comments today solely reflect my own views. I plan to discuss 3 issues:

(1) The importance of treating anemia in kidney disease patients, (2) the optimal hemoglobin in patients with kidney disease, and (3) My support for bundling of epoetin and other injectibles into the dialysis composite rate to remove incentives for over-treatment.

1. Anemia of Chronic Kidney Disease

Anemia is highly prevalent among patients with chronic kidney disease (CKD). By the time patients develop advanced kidney disease over 60% are anemic and need treatment with an erythropoiesis stimulating agent (ESA). On dialysis, over 95% of patients require an ESA. Erythropoetin is the most costly drug for CMS/Medicare—accounting for over $2 billion.

There is a good body of evidence that supports anemia treatment—fewer transfusions and improved quality of life, upto a hemoglobin of 10 to 11 grams per deciliter. The recommended strategy for treatment of anemia is based on guidelines disseminated by the National Kidney Foundation and the FDA label for epoetin and darbepoetin.

2. The Optimal hemoglobin in patients with kidney disease, based on current evidence, should be no higher than 12 grams per deciliter, conforming to the FDA label.

Several randomized controlled studies, both in dialysis and in predialysis patients, demonstrate at best only modest benefit in quality of life and increased risk of cardiovascular complications and death in patients treated to a hemoglobin level that exceeds 12 grams per deciliter.

It is important to note:

a.) Studies that have shown benefit for cardiovascular outcomes or survival are retrospective and observational in design. There is broad consensus that even the best designed and conducted retrospective observational studies are inferior to randomized controlled studies.

b.) Randomized controlled studies that have looked at patients with kidney disease, whether on dialysis or not, i.e., in the aggregate, have demonstrated increased risk.

- The normal hematocrit study—increased risk for clotting of dialysis access, and risk of death or heart attack
- The Canada-Europe study—increased risk of stroke
- The CHOIR study: a hazard ratio of 1.34 (or a 34% higher risk) of death and cardiovascular complications.

The higher rate of composite events was explained by a higher rate of death (48% higher risk, P=0.07) and heart failure hospitalization (41% higher risk, P=0.07). While quality of life showed improvement from baseline values in both groups it was similar between the two groups. However, more patients in the high hemoglobin group experienced least one serious adverse event compared to the low hemoglobin group.

- The CREATE study: an absolute increase in cardiovascular events and in the time to dialysis.

Whether one looks at studies focused narrowly on the dialysis population or on predialysis patients, signals for increased risk are evident with only very modest benefit in quality of life.The National Kidney Foundation (NKF) Kidney Disease Quality Initiative (KDOQI), the European Best Practice Guidelines for Anemia and the FDA have all considered both dialysis and pre-dialysis patients together. The data on the optimal hemoglobin level has been considered in the aggregate and applied to both populations.

Collectively, these studies demonstrated risk with normalizing the hemoglobin in patients with kidney disease on dialysis. The results reinforce the FDA label for epoetin of not recommending hemoglobin levels of greater than 12 grams per deciliter in patients with kidney disease. A final point, it is reassuring that the FDA is empowered with evaluating the efficacy and safety of drugs in the United States. The primacy of the FDA in regulating epoetin therapy in the United States should be maintained.

Hemoglobin levels among Dialysis Patients in the United States

Despite the FDA label, the United States Renal Data System (USRDS) a large federally funded registry of patients on dialysis, in its 2006 report indicates that more than 40% of dialysis patients have a hemoglobin level greater than 12 g/dL. Over 20% have hemoglobin levels above 13 g/dL.

The explanations provided for this include the inability to target a narrow range of hemoglobin because of a phenomenon termed hemoglobin cycling and that patients have excursions in hemoglobin levels beyond the 12 grams per deciliter range for only a very brief period of time. However, achieving the FDA recommended range is achievable by some dialysis chains. Only 30% of patients dialyzed at Davita facilities have hemoglobin levels of less than 12 grams per deciliter, whereas over 80% of DCI patients are able to maintain their hemoglobin level at less than 12 grams per deciliter. As well, USRDS data suggests that excursions over 12 g/dL may occur for 3 or more months. The strategy of targeting patients using higher epoetin doses to a higher hemoglobin with these transient excursions could be harmful.

The use of subcutaneous epoetin has been clearly shown to result in the use of approximately 1/3rd less epoetin yet only a small minority of dialysis facilities use the subcutaneous route for epoetin administration.

Despite CMS reimbursement changes, or because of them, data suggests that the proportion of patients outside of the FDA label appears to be increasing—some have termed the reason for this as being driven by “perverse incentives”.

3. Bundling of injectibles, including epoetin, offers several benefits and ought to be adopted.

The bundling of injectible drugs into the reimbursement of the dialysis procedure, i.e., into the composite rate offers several benefits and should be adopted.

a.) It removes incentives for over-treatment—aiming for higher hemoglobin levels using higher and higher doses of epoetin.
b.) It will likely reduce the escalating costs for injectible drugs, particularly epoetin, in the treatment of dialysis patients.
c.) It will encourage the use of subcutaneous administration of epoetin—a practice widely used in Europe, Canada, and in our own VA system. This should facilitate lower doses of epoetin in the treatment of anemia.

Summary:

I recommend that the importance of following the FDA label for epoetin in the treatment of anemia of kidney disease should be followed.

a.) **The hemoglobin target should not be greater than 12 grams per deciliter as iterated in the FDA label.**
b.) **Medicare should modify its reimbursement policy to comply with the FDA label. Adopting a bundled reimbursement schedule will likely remove the incentive for higher epoetin use and should increase subcutaneous administration of epoetin**.

The Target Hemoglobin in Patients with Chronic Kidney Disease

Introduction

Anemia is highly prevalent among patients with chronic kidney disease (CKD) (1). Treatment of CKD anemia with erythropoietin has been shown to enhance quality of life (2,3), however, evidence supporting a benefit of anemia correction in improving cardiovascular morbidity and mortality has been limited and based largely on observational studies and smaller interventional trials (4–6). These studies have demonstrated an association of high hemoglobin (>12.0 g/dL) with a lower rate of cardiovascular morbidity and death (5,6). However, as others have pointed out elsewhere, observational studies have limitations (7,8). Primarily, observational designs are unable to easily adjust for the effect of confounding. Indeed, Parfrey has recently pointed out that survivor bias could be an important reason for explaining the discordant findings between observational studies and randomized controlled trials in anemia (7). Related to this, Cotter and colleagues have also presented data suggesting that the hemoglobin level per se may not be a valid surrogate outcome in assessing the true effect of anemia correction in kidney disease patients (8). A further problem with the published studies has been that assessment of quality life may be limited by the open label design of some studies or have used quality of life instruments that have not been adequately validated in kidney disease patients (9). The purpose of this article is to critically appraise these studies in an attempt to arrive at some conclusions about the optimal target hemoglobin in CKD patients.

Randomized Studies show No Benefit of a Higher Hemoglobin level

Several randomized controlled studies have been published thus far (10–15). With the exception of two studies, the Normal Hematocrit Study (10) and the Canada-Europe Study (11), observations have been limited by the sample size used or premature discontinuation of the study. The Normal Hematocrit study was a randomized controlled study of hemodialysis patients with established heart disease comparing a hematocrit target of 42% to 30%. The study was stopped by the Data Safety Monitoring Board because of a higher rate of vascular thrombosis in the patients randomized to the higher hematocrit group. However, the patients in the higher hematocrit group also had a higher, although not statistically significantly higher, rate of non-fatal myocardial infarction (MI) and death. Several explanations were entertained to explain these findings. These included: the possibility of very high hematocrit's in the higher hemoglobin group resulted in hemoconcentration and therefore thrombosis, greater use of iron, and a lower dialysis dose. The Canada-Europe study also randomized hemodialysis patients to a higher versus lower hemoglobin (hemoglobin values of 13.0 versus 11.0 g/dL, respectively). However, in contrast to the Normal Hematocrit Study, Parfrey et al selected patients that were not at high risk of cardiovascular disease by excluding patients with symptomatic heart disease as well as those with left ventricular dilatation at baseline. Moreover they enrolled incident dialysis patients. While they did not evaluate hard endpoints such as death, or myocardial infarction, or stroke, they did evaluate changes in cardiac geometry (left ventricular volume index (LVVI) and left ventricular mass index

(LVMI). Moreover, they assessed heart failure and quality of life. No significant benefit in either of the cardiac structural or functional parameters was observed in the high versus low hemoglobin groups. However, a statistically significantly higher rate of cerebrovascular accident in the higher hemoglobin group was observed on secondary analysis. Quality of life did show an important difference in the high versus lower hemoglobin group with respect to the Vitality score, which was improved over time in patients randomized to the higher hemoglobin. In this regard, the Canada-Europe results were concordant with the Normal Hematocrit Study that also showed improvement in specific quality of life domains in the high versus low hematocrit groups.

Hemoglobin Variability Necessitates a Broader Hemoglobin Range

An important problem with setting hemoglobin targets has become apparent from recent studies that have evaluated the variability of hemoglobin levels in patients on epoetin treatment in the dialysis setting. Three studies collectively suggest that it is difficult to maintain the hemoglobin level in the 11 to 12 g/dL range (16–18). In the study by Fishbane et al >90% of dialysis patients studied experienced hemoglobin cycling (16). These investigators reported that the mean number of hemoglobin excursions was 3.1 ±1.1 per patient/year. The mean amplitude per hemoglobin excursion was 2.51 ±0.89 g/dL, and the mean duration of hemoglobin excursions was 10.3 ±5.1 weeks. Indeed, the NKF Work Group has "rejected, identifying a target hemoglobin level bounded by narrow upper and lower values (e.g., 11.0 to 12.0 g/dL) (15). Such a target affords neither clarity nor simplicity, is possible to achieve in only a minority of patients, discourages flexibility in managing individual patients, and likely promotes cycling of hemoglobin results greater than and less than the target."

Recent New Data from Randomized Controlled Trials

The recent publication of the CHOIR and CREATE studies informs the debate regarding the target hemoglobin level in CKD patients (19,20). CHOIR was an open-label,randomized trial that studied 1432 patients with CKD: 715 patients randomized to receive epoetin alfa targeted to achieve a hemoglobin of 13.5 g/dL, and 717 were randomized to receive epoetin alfa targeted to achieve a hemoglobin of 11.3 g/dL (19). The median study duration was 16 months. The primary end point was a composite of death, myocardial infarction, congestive heart failure (CHF) hospitalization (excluding hospitalization during which renal replacement therapy occurred), and stroke. Two-hundred-twenty-two composite events occurred: 125 events among the high hemoglobin group and 97 events among the low hemoglobin group P=0.03, hazard ratio of 1.34; with 95 percent confidence interval of 1.03 and 1.74. The higher rate of composite events was explained largely by a higher rate of death (48% higher risk, P=0.07) or CHF hospitalization (41%, P=0.07). Although neither death nor CHF hospitalization were statistically significantly higher in the higher versus lower hemoglobin group, the study was not powered for this purpose. While quality of life showed improvement from baseline values in both groups and were similar between the two groups. However, more subjects in the high hemoglobin group experienced least one serious adverse event compared to the low hemoglobin group. The Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin beta (CREATE) study enrolled approximately 600 patients. Subjects were randomized to an early anemia correction or a late anemia correction group (20). The early anemia correction group received epoetin beta therapy immediately for a target hemoglobin 13–15 g/dL. The late anemia correction group did not receive treatment until their hemoglobin is >10.5 g/dL; their target hemoglobin was 10.5–11.5 g/dL. The study showed that "complete correction" was not associated with a statistically significantly higher rate of the first cardiovascular event (58 events in the high hemoglobin group versus 47 events in the low hemoglobin group; hazard ratio of 0.78, 95% confidence interval, 0.53 to 1.14; P=0.20). However, left ventricular mass index remained stable in both groups but dialysis was required in more patients in the higher versus lowed hemoglobin group (127 vs. 111, p=0.03). On the other hand, unlike CHOIR, in CREATE a quality of life benefit, at least in year 1 of the study, was observed for the higher versus lower hemoglobin group.

Therefore, both studies showed either risk or no benefit in aiming to completely correct the hemoglobin in CKD patients, not receiving dialysis. The CHOIR study was larger and showed a statistically significant difference for the primary endpoint, whereas the CREATE study was much smaller and showed a trend for increased risk but did not reveal statistically significant differences for the primary endpoint. It is important to note that, unlike the Normal Hematocrit or Canada-Europe studies, both CHOIR and CREATE evaluated pre-dialysis CKD patients and so the results may not be generalizable to the dialysis community. However, both the Normal

Hematocrit and the Canada-Europestudies in dialysis patients also demonstrated either no benefit or increased risk. Collectively, this data strongly suggests that the most prudent course is to partially correct the hemoglobin in all chronic kidney disease patients, whether on dialysis or not, until more data is available in future studies.

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Chairman THOMAS. Thank you very much, Dr. Singh.
Mr. Cotter.

STATEMENT OF DENNIS J. COTTER, PRESIDENT, MEDICAL TECHNOLOGY AND PRACTICE PATTERNS INSTITUTE, BETHESDA, MARYLAND

Mr. COTTER. Chairman Thomas, Congressman Rangel, Congressman Stark, distinguished members. Good morning. I am Dennis Cotter, President of the Medical Technology and Practice Patterns Institute. I appreciate the opportunity today to talk about patient safety and quality issues. We have studied clinical outcomes of ESRD patients for more than 10 years. For almost two decades great controversy has surrounded the anemia treatment management goal; that is the target hematocrit. During this time, they have increased hematocrit from 33 percent to 37.5 percent; most recently to 39 percent and higher. Were these charges warranted? The answer to this question became clear when results of new clinical trials joined with earlier clinical trials demonstrated that patients targeted to higher hematocrit levels have increased mortality and many other adverse side effects. Through the current rules which endorse expanding EPO reimbursement to allow hematocrit to be targeted to any level, CMS has implemented a policy that can be harmful to its beneficiaries and will cost hundreds of millions of dollars in additional expenditures.

For some patients, it takes a small amount of EPO to elevate EPO hematocrit. For others, it takes a large amount. Clinical trials have shown that those targeted to high hematocrits and high EPO doses have higher mortality rates to those targeted to low hematocrit and low EPO doses. Because the population is made up of both EPO responders and EPO non-responders, the question remains whether patients who experience higher mortality rates were predominantly EPO responders or non-responders.

It is unlikely that industry sponsored research will answer this important question. Answering this question is the subject of our ongoing NIH funded research that addresses the concern that EPO therapy itself might contribute to harmful outcomes. Current CMS policy and industry sponsored clinical practice guidelines support both high target hematocrit and high EPO doses, assuming that high hematocrits improve outcomes, an assumption that is contrary to clinical trial. To date, no normal assessment of the appropriate dosing level has been conducted nor has a payment policy been implemented to encourage optimal dosing. Removal of a profit incentive by adding EPO to the composite rate should reduce over utilization and would also encourage research to determine optimal dosing. CMS policy appears to be heavily weighted on both the opinion and the notion that hematocrit variability is the overriding problem. As a result, this has encouraged EPO over-utilization, driving higher Medicare payments. Given the new policy, which opens up the upper limit of the target hematocrit, it is anticipated that providers will respond to the financial incentive with even more aggressive use of EPO.

Our recommendations: Adhere to the FDA label until further studies clarify the causal link between EPO, hemocrit and patient outcomes. Following FDA dose titration recommendations should be sufficient to maintain hematocrits within the 30-36 percent hematocrit range, deemed to be the safest range for all patients.

Treatment guidelines and reimbursement policies must put restrictions on the level of EPO dose, if necessary.

Further studies are needed to study patients that are hyporesponsive to high EPO doses. Regarding EPO and for all future drug evaluations, avoid the over reliance on observational studies, often industry sponsored as opposed to rigorously controlled randomized clinical trials. It is imperative that EPO coverage decisions adhere to established hierarchy of evidence that focuses primarily on RCTs and systematic reviews.

Finally, promote research which is independently funded rather than industry sponsored for the development of treatment guidelines and payment policies.

Thank you for your consideration of our concerns.

[The prepared statement of Mr. Cotter follows:]

Statement of Dennis J. Cotter, President, Medical Technology and Practice Patterns Institute, Inc., Bethesda, Maryland

Chairman Thomas, Congressman Stark, distinguished Committee members, good morning. I am Dennis J. Cotter, President of the Medical Technology and Practice Patterns Institute. I appreciate the opportunity to talk about patient safety and quality issues. We have studied clinical outcomes of ESRD patients for more than 10 years.

For almost two decades, great controversy has surrounded the anemia management treatment goal, that is, the target hematocrit. During this time, CMS has increased hematocrit targets, from 33% to 37.5%, and most recently, to 39% and higher. Were these changes warranted? The answer to that question became clear when results of new clinical trials, joined with earlier trial results, demonstrated that patients, targeted to higher hematocrit levels, have increased mortality and many other adverse side effects. Through the current rules which endorse expanding EPO reimbursement to allow hematocrit to be targeted to any level, CMS tacitly has implemented a policy that can be harmful to its beneficiaries and will cost hundreds of millions of dollars in additional expenditures.

THE SCIENCE

For some patients, it takes a small amount of EPO to elevate the hematocrit (EPO responders) and, for others, its takes a large amount (EPO non-responders). Clinical trials have shown that those targeted to high hematocrits and high EPO doses have higher mortality rates than those targeted to low hematocrits and low EPO doses. Because the population is made up of both EPO responders and EPO non-responders, the question remains whether patients who experienced higher mortality rates were predominately EPO responders or EPO non-responders. It is unlikely that industry-sponsored research will answer this important question. Answering this question is the subject of our on-going NIH funded research which addresses the concern that EPO therapy, itself, might contribute to harmful outcomes. Current CMS policy and industry-sponsored clinical practice guidelines support both high target hematocrit and high EPO doses, assuming that high hematocrits improve outcomes, an assumption that is contrary to clinical trial results. To date, no formal assessment of the appropriate dosing levels has been conducted, nor has a payment policy been implemented to encourage optimal dosing. Removing the profit incentive, by adding EPO to the composite rate should reduce over-utilization and would also encourage research to determine optimal dosing.

THE POLICY

CMS policy appears to be heavily weighted both on opinion and on the notion that hematocrit variability is the over-riding problem. As a result, over the years this policy has encouraged EPO over-utilization, driving higher Medicare payments. Given the new policy, which opens the upper limit of the target hematocrit, it is anticipated that providers will respond to the new financial incentive with even more aggressive use of EPO.

WHERE WE GO FROM HERE

Our recommendations are the following:

- Adhere to the FDA-approved label until further studies clarify the causal link among EPO, hematocrit, and patient outcome. Following FDA dose titration rec-

ommendations should be sufficient to maintain hematocrits within the 30–36% hematocrit range, deemed to be the safest range for all patients.
- Treatment guidelines and reimbursement policies must put restrictions on the level of EPO dose, if necessary. Further studies are needed of patients who are hypo-responsive to high EPO doses.
- Regarding EPO, and for all future drug evaluations, avoid over-reliance on observational studies, often industry-sponsored, as opposed to rigorously controlled randomized clinical trials. It is imperative that the EPO coverage decisions adhere to established hierarchy of evidence that focuses primarily on RCTs and systematic reviews.
- Promote research which is independently funded, rather than industry-sponsored, for the development of treatment guidelines and payment policies

Thank you for your consideration of our concerns.

Chairman THOMAS. Thank you all very much.

I will ask a couple of questions and urge my colleagues to focus their responses as well. History is history, but we now have some fairly clear evidence. Can you think of a worse system to treat patients with End Stage Renal Disease than having facilities offering the service not getting updates or cost-of-living adjustments but in fact a fixed dollar payment for years and having a drug which is a significant assistance in a monopoly situation with no competitive pricing structure being available and, in fact, encouraged in terms of increased uses. Now we see clearly beyond what most people are now beginning to believe would be appropriate standards. What would we add to that to make it worse than the structure we now have? Is there anything we are missing in terms of policy that could make sure that we don't endanger these people even more?

Mr. COTTER. This is a recipe for disaster. That is why we are here today. EPO dosing is a—it is done under the notion that the drug does no harm. Because of that notion, there is a very aggressive attitude toward using high doses of EPO to continue.

Chairman THOMAS. That, my understanding, is the way it is administered, in terms of not allowing any new or inventive approaches, for example subcutaneous, in terms of advantages. There is no ability to continue to move toward better practices within the structure that we have established, i.e., there is no incentive and I don't think anyone should focus on the people who are running these services and who are doing the best job they can. It is the structure under which they are operating these services that don't allow them to move into those. Is that an appropriate statement?

Mr. COTTER. This is viewed as an income stream. If it was viewed by providers as a cost, then the incentive would be to provide optimum dosing as does the VA. The VA doses using the subcutaneous route, and that, within the VA, EPO treatment is viewed as a cost. So, if you change the incentives around, you will motivate providers to become much more efficient.

Chairman THOMAS. Dr. Singh, you made a statement about your study about comparisons with people who are not in end stage renal but obviously chronic kidney disease and other patients. Notwithstanding the exclusivity of drugs used in each of these areas, i.e. monopoly, did you find any difference, any significant difference that would require a maintenance of drugs dealt with in a different way for those populations, or was there sufficient commonality from your study that we should look at that was more of a com-

bined group and therefore possibly have an opportunity to deal with what is now a monopoly in the End Stage Renal Disease of administering of drugs?

Dr. SINGH. I agree with you. I think the study that we published as well as other studies do not provide sufficient evidence at the present time to distinguish treatment in one population versus the other. In other words, at this moment I think, like the approach taken by the FDA as well as by the National Kidney Foundation, it seems reasonable to consider these populations and studies on these populations in the aggregate and nothing—there has been no convincing evidence that has supported the idea of separating these populations out. There is no reason in my mind to think that the dialysis population will benefit from higher doses of EPO or from higher hemoglobin levels beyond what we have found in our studies. In fact two other randomized controlled studies support the notion of increased risk in the dialysis population.

Chairman THOMAS. Why was the CHOIR trial terminated?

Dr. SINGH. It was terminated because the Data Safety Monitoring Board saw evidence for increased risk for adverse risk in the higher hemoglobin group, and they found that there was going to be no likelihood of showing any benefit, and therefore, the DSMB terminated the study. We followed that recommendation.

Chairman THOMAS. The policies that were currently advocating under CMS are which end of the spectrum vis-a-vis the CHOIR trial? At the high end or the low end?

Dr. SINGH. The Medicare policy recommends there be a 25-percent reduction in the epoetin dose when the hemoglobin level hits 13 grams or hematocrit at 39 percent what's remarkable is that as recent, as the same week as the CHOIR study was published, one of the largest dialysis providers circulated a guideline for protocol for hemoglobin management which recommended only a 10-percent reduction in epoetin dose when the hemoglobin level reaches 13 grams and a 25-percent reduction when it reaches 14 grams or higher, so, clearly, even beyond what Medicare recommends and certainly well beyond what the CHOIR data suggests, which is considered safe. So, you are absolutely right. There is—not only does this study suggest increased risk beyond 13, beyond actually 12.5 because that was the achieved hemoglobin level. But Medicaid guidelines are at 13, where there is a reduction and dialysis providers are even flaunting that and going for higher levels still.

Chairman THOMAS. It is in large part because of the payment system and the structure we are dealing with and some incentives of the structure.

Can you give us—is there agreement between the three of you and more than the decade long study and others that would give us one, two, three fairly simplified steps that we could take that could at least get us significantly in a different direction? Can you give it to me in just a few terms? Obviously, you have advocated bundling. Are there any other suggestions?

Dr. SINGH. I would recommend they should be—risk adjustment of the population has been recommended by CMS because these are complicated sick dialysis patients and we do not want to actually disincentivize the treatments of patients who are sick.

Chairman THOMAS. I understand that. Have you read the GAO study?

Dr. SINGH. Yes.

Chairman THOMAS. One of the concerns that we have that we will be presented shortly is we have made recommendations; we have demanded certain aspects. The argument has been that we have not been able to develop them.

Thank you very much.

Mr. Rangel.

Mr. RANGEL. Thank you so much for sharing your views with us.

Could you tell us, why in the world would the CMS have a policy that differs from with the GAO, the FDA, the National Kidney Foundation, the National Institutes of Health, the providers of health care, as to why they would want to encourage through policy the overuse of a drug that places peoples' lives at risk and even death and is more costly to the Federal Government? Now just try to think of any reason why any agency or department of the Federal Government would want to do this.

Mr. COTTER. Yes, I think, from my understanding of this, we wrote a policy analysis of this and published in the Health Affairs Journal, is that there is a notion that the policy must impress hematocrit variability. However, that is driven by aggressive dosing so it is a self-fulfilling prophecy. If you raise the hematocrit target, you encourage more aggressive dosing which in turn raises more variability. That is the only argument that CMS has had that they have claimed that the policy is based on. They have claimed that there is no science to support these high levels. It is only this issue that is non-scientific of hematocrit variability.

Dr. PIZZI. Mr. Cotter used the word notion. The notion has been in the dialysis community for several years that the higher the hemocrit, the better the outcome. Even the National Kidney Foundation updated their guideline this year to increase the upper hemoglobin limit to 13 without founded evidence to support that. Now the results of the trials testing these levels doses are starting to come back, and, in fact, we have found out that 13 is too high. CMS, as well as the National Kidney Foundation, I believe and I agree with Mr. Cotter and Dr. Singh that it is time to revert back to the label, which is a hemoglobin of 10 to 12.

Dr. SINGH. I think we have limited presentation at the present time as to why this occurs and whether it is related to factors such as high dosing or frequent measurement of hemoglobin. Nevertheless, we certainly should seek increased risk of hemoglobin levels that are beyond the current label of the drug and my advice would be that we take greater pains and I think CMS takes greater pains to ensure that the population of dialysis patients that this represents a vulnerable population of hemoglobin levels that are below that level until we get more data, until more studies are published to indicate this is a—that the alternative is a reasonable strategy.

Mr. RANGEL. Thank you. Mr. Chairman, I want to congratulate you for the order of the witnesses, to have the experts testify early. Whether we can establish this as some kind of a policy, that makes it easier for us.

Chairman THOMAS. I appreciate the gentleman. I am doing this for pure convenience of members in a very extreme time, and I don't intend to make any kind of a precedent. I am walking out the door in a few days, and you can deal with it on your own time.

The gentlewoman from Connecticut wish to you inquire.

Ms. JOHNSON OF CONNECTICUT. How easy is it to achieve stability in a patient to—how big an issue is this hematocrit variability? I gather from you that we really don't know enough to actually keep a patient stable at 12, or we would be doing it.

Mr. COTTER. We have done a study of this because we wanted to prepare something for this hearing. It is simply that if you maintain a prudent dosing strategy as recommended in the FDA labeling, you start off in small doses and you tritiate up until the patient responds to the drug, you do not have this variability. What providers are doing now, they are starting with very high doses beyond the FDA label and these patients, some of them overshoot. Some don't. Remember, I said we have responders and non-responders to EPO therapy. So, for those both responders and non-responders, they get the same dose.

Ms. JOHNSON OF CONNECTICUT. Thank you. So, the variability issue can be addressed by titrating up, and if you do that, then there is no difference in frailty or nature of the patient as to how variable, how much their swings and their hemocrit levels as you dose.

Mr. COTTER. That is why you want to titrate up.

Ms. JOHNSON OF CONNECTICUT. Once you get there, are there still those swings?

Mr. COTTER. There could be swings, sure. But the FDA label says that the target should be 30 to 26, so that allows the swings.

Ms. JOHNSON OF CONNECTICUT. So, you think the swing being allowed to go up to 13 is too big a swing?

Mr. COTTER. Absolutely.

Ms. JOHNSON OF CONNECTICUT. How effective has the CMS new payment policy adopted in April been in at least bringing down dosing above 13?

Mr. COTTER. Well, according to the GAO report, I will let them tell you about that, but it looks like dosing is migrating up slightly right now, but they are reporting an average dose. That means there are some patients on the high end of that average are getting very high doses.

Ms. JOHNSON OF CONNECTICUT. On the bell curve, their new payment policy penalizes high doses of patients that are at 12/13, and my understanding is, we will hear more from the next panel, but that has brought down the outliers. Is that your understanding?

Mr. COTTER. I would like to hear CMS defend that because, in October of this year, they virtually annihilated that restriction. It is basically not there any longer.

Ms. JOHNSON OF CONNECTICUT. The 25 percent payment cut?

Mr. COTTER. I don't know how a contractor could implement that direction that they are giving him, and by the way, the target is not even 39 percent. It could go higher. It can go to 42. It can go to 50. There is no higher bound.

Ms. JOHNSON OF CONNECTICUT. But there are payment cuts——

Mr. COTTER. The only payments cut is that, if a monthly dose goes over 500,000 units per or more, which is 5 to 10 times above the FDA label; it is bizarre.

Chairman THOMAS. Thank you.

Mr. Stark, do you wish to inquire.

Mr. STARK. I want to thank the panel for all of the work they have done in this area. I have a couple of, I guess, less technical questions.

But my understanding is that if we—I can't pronounce subcutaneous, but I am going to ask Dr. Pizzi, if we inject the drug, then we might be able to use about 30 percent less; is that correct?

Dr. PIZZI. That is true. There are numerous studies that indicate that. That is one of the standard ways to introduce savings because the drug essentially acts as a depot.

Mr. STARK. Could the makers of the drug make it more comfortable for us who don't like getting stuck?

Dr. PIZZI. The key is that to make it more comfortable, the clinics have a multi-dose vial which has a benzyl-alcohol in it, and that reduces some of the stinging. There are other techniques that can be used to reduce discomfort, too.

Mr. STARK. I am all for that.

Then the other question is, would it make any sense, Dr. Singh, if you know, in paying for the application of this drug as it is now used in the dialysis system, why we should pay more than a dollar per application, not counting the cost of the drug? It is just dumped in the system, I gather, and takes no particular—nothing more than adding it to the mix. Is that a fair layman's description of how you would add this if you are not injecting it?

Dr. SINGH. I think that is, sir. It is a little bit more complicated than just adding it. I think that there is a significant—there is a significant amount of work that goes in to the administration in a safe manner to prevent——

Mr. STARK. Even when it is done as——

Dr. SINGH. Even when it is done as part of it. So, I don't think I would advocate the idea that we just add it in a sort of routine manner. However, I would just add that the notion that we can give it subcutaneously is not a bad idea. After all, our veterans in this country received this drug subcutaneously largely. People in Europe and people in Canada. So, I do agree that it is—there is some discomfort giving it subcutaneously, but it is certainly good enough for some of our finest people.

Mr. STARK. We are talking about saving 600 million bucks a year, which is not chump change.

Final question, Dr. Singh. With all of this recent information about overdosing things, how have you changed both your own practice, and at Brigham Young, how are you changing what you teach your residents or interns?

Dr. SINGH. I am the medical director of a dialysis unit in Boston. We have instituted a new protocol to ensure that the patients' hemoglobin levels stay below the—to the degree we can help it below 12 grams per deciliter. The USRDS shows that chain in which I practice has 80 percent of their patients that are below 12

grams per deciliter in contradistinction to other dialysis providers who have higher proportional patients.

We have also instituted modifications for our health care system partners, health care in Boston, to try to ensure that we follow the FDA label. Certainly teaching people out there both at the American Society of Nephrology and elsewhere, I certainly advocate the notion that we should follow the FDA level and stay below 12 grams per deciliter.

Mr. STARK. There is always the danger of underdosing. We certainly don't want to have payment practices that would encourage that. But in the general practice in dialysis today, how would you rank the danger of overdosing as a—or underdosing? Is there as much danger in underdosing as overdosing?

Dr. SINGH. I think the biggest problem currently is the fact that patients are coming to dialysis still who have never ever been treated with epoetin and should be. So, certainly, we could increase the awareness with the population with increasing treatment well before they start dialysis. However, I do not believe that underdosing will be as much of an issue as much as overdosing, especially since the studies now show continued increased risk.

Chairman THOMAS. Did I hear you say, Dr. Singh, given the current payment system and the structure of the monopoly drug, that you are following a policy which reduces the income to those dialysis centers that you are involved with?

Dr. SINGH. We have taken the approach that we will follow what is appropriate from a clinical standpoint, and if that means that we get paid less, that is appropriate. But we want to make sure that we treat patients to a level of hemoglobin——

Chairman THOMAS. I understand that, but what you have done is made a conscious decision based upon your knowledge not to follow a system which you could easily follow. Wouldn't it make a whole lot of sense to change the system so you don't have to make that decision?

Dr. SINGH. Yes, sir. I agree with you.

Chairman THOMAS. Any additional questions?

Mr. CAMP. I don't have a question. I want to associate with your remarks.

Mr. LEWIS OF GEORGIA. Mr. Singh, I understand that 30 percent of dialysis patients are African-American, but yet we are only 8 to 12 percent of the total population. These numbers are not improving, and we are not seeing any improvement in keeping patients off of dialysis. What do you need from Congress to help prevent patients from going on dialysis? In the minority community, what needs to be done to address this disparity.

Dr. SINGH. Thank you, sir. Recent data from the—published from the United States Renal Data System from the NIH suggest there may be a leveling off of the incident rate of patients starting dialysis. But the—but your point is well taken. We still have an unsatisfactory number of people starting dialysis in the United States, and it is over-representative of minorities, particularly African-Americans. We also have no change in the mortality or no significant change in the mortality of patients on dialysis.

If you ask me, what we need to do is to increase the greater funding to the NIH so that independent research can be performed

by investigators in the United States to understand what factors increased the risk of progression of patients, particularly African-Americans, to dialysis; what are the factors that account for this very high risk of cardiovascular disease among dialysis patients; as well as studies on anemia, to try and truly understand this issue of hemoglobin cycling and why there is this excess risk should be funded by Congress. I think we need—we certainly need more money funded through the appropriate channels through the NIH to fund more studies.

But I certainly agree with you that African-Americans represent a disproportionate amount of people on dialysis, and the mortality of these people have not changed significantly over the past decades. So, we do need help, and we need help in terms of funding in the research community to gain a great understanding and develop better strategies.

Chairman THOMAS. Thank the gentleman. We are calling it End Stage Renal Disease, and what we really need to put emphasis on is prevention and education so they never reach the end stage along with the additional study that you are making, and frankly, that doesn't take an NIH study. That takes talking about diet, lifestyle and the rest.

Thank you very much for your research.

Again, it is quite amazing that, all of a sudden, in a couple of months, significant research is coming out focusing on this issue. I assume that there is going to be continued examination of this. Obviously, we need all the help we can get in terms of not only understanding the application of these drugs that are literally miracle drugs but the manner in which we provide it to people who provide the service and in fact the taxpayers pay for it. Thank you very much.

I would now ask the second panel to please come before us. The Chair is conscious of the time restraints on very busy people.

The Chair is pleased to have, once again, the Honorable David M. Walker, and I would like to welcome Leslie Norwalk, who is the new Acting Administrator for the Centers for Medicare and Medicaid Services. Thank you very much for attending.

Dr. Walker, obviously, you have just concluded the study. Again, interestingly, all of this is coming together at the same time, and we have it available if anyone hasn't seen a copy of it. I do think it is very useful, and as is customary, any testimony that you have written will be made a part of the record, and you can address us in any way you see fit in terms of what we now have before us in the GAO study.

STATEMENT OF THE HONORABLE DAVID M. WALKER, COMPTROLLER GENERAL, U.S. GOVERNMENT ACCOUNTABILITY OFFICE

Mr. WALKER. Thank you, Mr. Chairman. I appreciate the opportunity to be here today to participate in the hearing on Medicare patients with End Stage Renal Disease. Let me also note, happy birthday and all of the best to you in retirement from the Congress.

As you know, from a broader perspective, the level and growth of Medicare spending combined with the over $30 trillion-plus amount of unfunded obligations for Medicare serves as evidence

that the current program is unsustainable in its present form. Furthermore, Medicare's sheer size and complexity make it vulnerable to improper payments and inefficient payment systems. Over the years, the GAO has worked with this Committee to try to address these challenges. CMS has taken a number of related efforts, and some progress clearly has been made, but as most GAO reports note, more remains to be done.

With regard to End Stage Renal Disease drug reimbursements, the GAO report which you held up—and I have a copy as well that you requested—points to ways to improve the efficiency of Medicare's payments in connection with the End Stage Renal Disease program. Over the years, we have observed that bundled payments tend to be more efficient than paying for services one at a time. Bundled payments cover a range of services delivered to the patient. As such, they give providers an incentive to furnish only those services that patients truly need because providers can not prosper by providing extra services.

Today's hearing focuses on End Stage Renal Disease paid under part B of Medicare. But one has to look at the whole part of part B to see the inefficiencies inherent in paying for services one at a time. Spending for physician services and other part B services over the past several years has been growing at an alarming rate. It is essential that Congress find ways to restructure payments to institute necessary efficiencies and control spending growth while maintaining quality and assuring patient safety.

Our report on End Stage Renal Disease drug payments observes that the current method of setting drug payment rates is an improvement over the previous system. However, it does not provide appropriate incentives. It does not control the incentive to over-utilize such drugs. The system in place pays providers the manufacturers' average sales price for the drug, plus 6 percent. Any system that provides for cost-plus payments provides an incentive for related parties to provide unnecessary care and extra services. Indeed, this is one of the reasons that the Congress changed Medicare's inpatient hospital payment to a bundle payment system in the mid-eighties.

We also observed in our report that Medicare's End Stage Renal Disease drug payment is dominated by a single drug, Epogen, which for several years has been Medicare part B's highest spending drug, approximately $2 billion in 2005. We also expressed concerns that there are currently no direct competitor drugs in the End Stage Renal Disease market. The lack of effective price competition could be having considerable adverse effects on Medicare's overall spending. Furthermore, the lack of significant efforts to verify the accuracy of the average sales price for drugs that are separately billable under part B is also a matter of concern, and that goes beyond End Stage Renal Disease.

Finally, returning to the bundling theme. We observed that, currently, congressionally mandated research on creating a bundled system for End Stage Renal Disease services, including drugs, has been delayed. The research being conducted by CMS would, among other things, ensure that providers are appropriately compensated for variations of complexity in patients' treatment. While this is important, we do not believe it is necessary or desirable to delay

movement to a bundled rate for End Stage Renal Disease services any longer than absolutely necessary. For this reason, we have suggested that Congress consider mandating the establishment of a bundle payment system for all ESRD services, including drugs, as soon as possible.

Mr. Chairman, this concludes my prepared remarks. I look forward to responding to your questions.

Thank you.

[The prepared statement of Mr. Walker follows:]

Statement of The Honorable David M. Walker, Comptroller General, U.S. Government Accountability Office

Mr. Chairman and Members of the Committee:

I am pleased to be here to discuss highlights from our report entitled *End-Stage Renal Disease: Bundling Medicare's Payment for Drugs with Payment for All ESRD Services Would Promote Efficiency and Clinical Flexibility*.[1] The report examines Medicare payments for certain drugs provided to patients with end-stage renal disease (ESRD), a condition of permanent kidney failure.[2]

Through Medicare's ESRD benefit, patients receive a treatment known as dialysis, which removes excess fluids and toxins from the bloodstream. Patients also receive items and services related to their dialysis treatments, including drugs to treat conditions resulting from the loss of kidney function, such as anemia and low blood calcium. The Centers for Medicare & Medicaid Services (CMS), the agency that administers the Medicare program, divides ESRD items and services into two groups for payment purposes. In the first group are dialysis and associated routine services—such as nursing, supplies, equipment, and certain laboratory tests. These items and services are paid for under a composite rate—that is, one rate for a defined set of services. Paying under a composite rate is a common form of Medicare payment, also known as bundling. In the second group are primarily injectable drugs and certain laboratory tests that were either not routine or not available in 1983 when Medicare implemented the ESRD composite rate. These items and services are paid for separately on a per-service basis and are referred to as "separately billable."

Over time, Medicare's composite rate, which was not automatically adjusted for inflation, covered progressively less of the costs to provide routine dialysis services, while program payments for the separately billable drugs generally exceeded providers' costs to obtain these drugs. As a result, dialysis facilities relied on Medicare's generous payments for separately billable drugs to subsidize the composite rate payments that had remained nearly flat for two decades. In addition, the use of the separately billable drugs by facilities became routine, and program payments for these drugs grew substantially. In 2005, program spending for the separately billable drugs accounted for about $2.9 billion. Medicare's payment for these separately billable drugs is the focus of my remarks today. My remarks are based on the information included in our aforementioned report.

Background

Since the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) was passed,[3] how separately billable drugs are paid for has changed—from payment based on each drug's average wholesale price (AWP),[4] to payment based on each drug's average acquisition cost, to payment based on the manufacturer's average sales price (ASP) for each drug. Specifically, beginning in 2006, payment for each drug is set at ASP + percent.

In recent years, CMS has been exploring, as required by the Congress, the creation of a bundled payment for all ESRD services, including the drugs that facilities

[1] GAO, *End-Stage Renal Disease: Bundling Medicare's Payment for Drugs with Payment for All Services Would Promote Efficiency and Clinical Flexibility,* GAO–07–77 (Washington, D.C.: Nov. 13, 2006).

[2] These drugs are covered under Medicare Part B, the part of Medicare that covers a broad range of medical services, including physician, laboratory, and hospital outpatient services and durable medical equipment. Part B-covered drugs are typically administered by a physician or other medical professional rather than by patients themselves. In contrast, drugs covered under the new prescription drug benefit, known as Part D, are generally self-administered by patients.

[3] Pub. L. No. 108–173, 117 Stat. 2066.

[4] Epogen, one of the separately billable drugs, was not paid under the AWP method. The method Medicare used to pay for Epogen was an amount set in statute for a single year—$10.00 per 1,000 units in 1994. CMS continued to pay this rate at its discretion until 2005.

currently bill for separately. In response to a mandate that CMS study the feasibility of creating a bundled payment,[5] the agency issued a study in 2003 concluding that developing a bundled ESRD payment rate was feasible and that further study of case-mix adjustment—that is, a mechanism to account for differences in patients' use of resources—was needed. In the MMA, the Congress required that CMS report on the design of a bundled prospective payment system for ESRD services, including a case-mix adjustment methodology, and conduct a 3-year demonstration to test the design of a bundled ESRD payment system.[6]

New Payment Provisions Reduced Subsidy from Separately Billable Drugs but Did not Eliminate Incentives to Overuse These Drugs

The effect of several legislative and regulatory changes since 2003 has been to raise the composite rate for dialysis services while reducing Medicare's pre-2005 generous payments for separately billable ESRD drugs. Under the first legislative change in 2005, Medicare expenditures for certain of these drugs dropped 11.8 percent. Under the current payment method, based on the ASP for each drug, Medicare's payment rates have varied from quarter to quarter but have remained relatively consistent with the lower 2005 payment rates.

The ASP-based rates are an improvement over the pre-MMA method, as ASP is based on actual transactions. However, certain unknowns about the composition of ASP and the ASP-based payment formula make it difficult for CMS to determine whether the ASP-based payment rates are no greater than necessary to achieve appropriate beneficiary access. For one thing, CMS has no procedures for validating the accuracy of a manufacturer's ASP, which is computed by the manufacturer. For another, CMS has no empirical justification for the 6 percent add-on to ASP. Regardless of how payment for these drugs is calculated, as long as facilities receive a separate payment for each administration of each drug and the payment exceeds the cost of acquiring the drug, an incentive remains to use more of these drugs than necessary.

The ASP payment method is of particular concern with respect to Epogen, which in 2005 accounted for $2 billion in Medicare payments and is Medicare's highest Part B expenditure drug. Introduced in 1989, Epogen—the brand name for epoetin alpha—was an expensive breakthrough drug used to treat anemia in patients with ESRD. Most ESRD patients receive injections of Epogen at nearly every dialysis treatment. Preliminary data for 2006 suggest that Epogen use, which grew rapidly in the years before the MMA provisions took effect, continues to grow, although at a slower rate than previously. Epogen is the only product available in the domestic ESRD market for anemia management. However, the ASP method relies on market forces to achieve a favorable rate for Medicare. When a product is available through only one manufacturer, Medicare's ASP rate lacks the moderating influence of competition. The lack of price competition may be financially insignificant for noncompetitive products that are rarely used, but for Epogen, which is pervasively and frequently used, the lack of price competition could be having a considerable adverse effect on Medicare spending.

Bundled Payment System for ESRD Services, Including Injectable Drugs, Would Promote Efficiency and Clinical Flexibility

Medicare's approach to paying for most services provided by health care facilities is to pay for a group—or bundle—of services using a prospectively set rate. For example, under prospective payment systems, Medicare makes bundled payments for services provided by acute care hospitals, skilled nursing facilities, home health agencies, and inpatient rehabilitation facilities. In creating one payment bundle for a group of associated items and services provided during an episode of care, Medicare encourages providers to operate efficiently, as providers retain the difference if Medicare's payment exceeds the costs they incur to provide the services. Medicare's composite rate for routine dialysis and related services was introduced in 1983 and was the program's first bundled rate.

Experts contend that a bundled payment for all dialysis-related services would have two principal advantages. First, it would encourage facilities to provide services efficiently; in particular, under a fixed, bundled rate for a defined episode of care,[7] facilities would no longer have an incentive to provide more ESRD drugs than

[5] Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000, Pub L. No. 106–554, app. F, § 422(b),(c), 114 Stat. 2763A–463, 2763A–516–517.

[6] Pub. L. No. 108–173, § 623(e),(f), 117 Stat. 2066, 2315–2317.

[7] In the case of the composite rate, one dialysis session constitutes an episode of care. Unlike the current composite rate payment method, a newly designed payment bundle could define the

Continued

clinically necessary. Second, bundled payments would afford clinicians more flexibility in decision making because incentives to prescribe a particular drug or treatment are reduced. For example, providers might be more willing to explore alternative methods of treatment and modes of drug delivery if there were no financial benefit to providing more services than necessary.

In the MMA, the Congress required CMS to issue a report and conduct a demonstration of a system that would bundle payment for ESRD services, including drugs that are currently billed separately, under a single rate. Any payment changes based on CMS's report or demonstration would require legislation.[8] Both the report, due in October 2005, and demonstration, mandated to start in 2006, are delayed, and CMS officials could not tell us when the report or results from the demonstration would be available.

In light of these circumstances, we have asked the Congress to consider establishing a bundled payment for all ESRD services as soon as possible. In our view, Medicare could realize greater system efficiency if all drugs and services were bundled under a single payment. A bundled payment would encourage facilities to use drugs more prudently, as they would have no financial incentive to use more than necessary and could retain the difference between Medicare's payment and their costs. To account for facilities' increased or decreased costs over time, a periodic reexamination of the bundled rate may be necessary. This would ensure that facilities would be paid appropriately and that Medicare could realize the benefit of any cost reductions.

Mr. Chairman, this concludes my prepared statement. I will be happy to answer any questions you or the other Committee Members may have.

Chairman THOMAS. Thank you.

Prior to going to Ms. Norwalk, because I know you have an important meeting to go to, if it is okay, and we will determine the length of the questioning perhaps like to just draw you out a bit in terms of your statement prior to moving to the CMS testimony.

As you know, I am very loathe to have Congress attempt to legislate the ways in which services are offered, but I want to understand in your underscore in your GAO in page 6 that in 2003 the Medicare Modernization Act required CMS to design a system that would no longer pay for each injectable ESRD drug in a separate rate. You then go on in the same paragraph to conclude CMS report is designing a report for bundled ESRD payment was due in September 2005. However, as of November of 2006, CMS officials could not tell us when the report would be issued. The demonstration testing the feasibility of a bundled rate mandated to start in July 2006 is also delayed.

If in fact this is what CMS has been doing, what is it that we are going to do as a Congress to put together a package which would answer those issues? You said perhaps it isn't as complicated as other others are talking about. What we heard from the previous panel is, there are drugs, and my understanding is they are identical, notwithstanding the fact they are used in separate purposes. The separate purposes are far closer together, if we can believe Dr. Singh's testimony, than we would have thought and that could possibly create a competitive model rather than a monopoly. Notwithstanding—since 2003—CMS can't put together a bundling package and present it to us based upon our requirements in

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episode of care more broadly. For example, the new payment bundle could cover dialysis and related items and services for 1 month.

[8] The MMA specified that drugs billed separately at the time the legislation was enacted continue to be billed separately and not bundled in the composite rate. MMA sec. 623 (d)(1), § 1881 (b)(13)(B), 117 Stat. 2314–15 (to be codified at 42 U.S.C. § 1395rr(b)(13)(B)).

MMA, what is it that you would be suggesting that we might do? That is what I am looking for.

Mr. WALKER. What I am suggesting is, there appears to be agreement that it makes sense to move to a bundled approval for payment for these drugs. And——

Chairman THOMAS. I believe the Congress certainly believes that.

Mr. WALKER. I believe that CMS believes that as well, and I think it is important that it is the Congress's will to say that while CMS needs to do demonstration work and while I think additional consideration needs to be given to drugs that are essentially identical or similar to Epogen that are not used in End Stage Renal Disease but are used for other purposes, I think it is important that the Congress's will be noted to say we expect you to move to bundled services by X date and you have to decide what X date is.

Chairman THOMAS. But we did, in essence, in 2003, while leaving it to the professional competence of CMS to move forward with that.

Mr. WALKER. My understanding is that you required something be done and a report be issued by a date certain rather than necessarily move to the bundled services by a date certain.

Chairman THOMAS. Okay. I think, possibly given the commonality of our position here, a more insistent direction with the specific date could produce something, but I will go back to the recent attempt to get letters answered and the dateline in terms of answering simple letters. So, to a certain extent, I appreciate the requirement to put a firm date, but I will tell you, I have no assurance that any firm date will be met.[11:45 a.m.]

Chairman THOMAS. If they cannot answer letters, I doubt if they are going to give us a program. That is my concern. Therefore, I also want to focus on how we can create a degree of competition and how we can create an opportunity to allow dialysis facilities to utilize various methods of infusion, injection, subcutaneous, others that are not absolutely dictated to by a policy that controls price and circumstances; and that perhaps is an area we might be able to move with, as well as bundling.

Mr. WALKER. Well, as you know, there is another drug company that is proposing to bring a drug to market that potentially would be used for End-Stage Renal Disease. There is litigation that is currently pending with regard to that. That was obviously beyond the scope of our study, but it is a fact, and so that is one possibility for competition.

Another thing that you touched on, Mr. Chairman, which I think is appropriate, is there are at least two drugs that are used, one of which is identical to Epogen and one of which is similar but not identical to Epogen. They are not used for End-Stage Renal Disease, but they are used for chronic kidney disease, and one would think that you could look at some of the pricing arrangements and other types of activities going on there. You are not requiring them to be used for End-Stage Renal Disease, but there is information there that I think would be relevant in determining, in effect, what should be paid for these drugs.

Chairman THOMAS. Thank you.

The gentleman from New York.

Mr. RANGEL. I have no questions. I just would like to thank you, Mr. Walker, for the dedicated service that you have provided over the years for the Congress and the country.

Chairman THOMAS. The gentlewoman from Connecticut, the Chairman of the House Subcommittee.

Ms. JOHNSON OF CONNECTICUT. Mr. Walker, did you look at the policy that CMS adopted in April?

Mr. WALKER. I apologize, Mrs. Johnson. My staff tells me that we looked primarily at the payment methodology. We looked at the policy, but we did not look at anything in depth other than the payment methodology. That is the really the only thing.

Ms. JOHNSON OF CONNECTICUT. Did you also look at why the demonstration has been slow to come together and the issue of risk adjusting in the demonstration? Dr. Singh did indicate that he thought risk adjustment was important. My understanding is that risk adjustment in a demo setting is an easy—I could be misinformed about that. I have not had time to do an in-depth development of my knowledge based on this issue. But I need to know why the demo has been hard to come together. While I will ask CMS that later on, since you are here and you gave this report I want to know, did you look at that?

Mr. WALKER. It is clear that the delay has in large part been due to considerations of looking at risk adjustment. We are not saying that that should not be done. We are not saying that you should discontinue the demonstration project either. We think it is important that that be done.

The bottom line point is this: It seems clear that Congress intended our work supports, and it is my understanding that CMS agrees, that we need to move to a bundled payment system as quickly as possible. I think the administrator is in a better position to answer why it has been delayed and when she thinks it is going to be completed. But for the interests of the patients and the interests of the taxpayers, I think we need to move to a bundled payment system as soon as possible.

Ms. JOHNSON OF CONNECTICUT. Thank you.

My concern is that the express purpose of the demonstration project was to demonstrate a bundled payment solution; and if risk adjustment is difficult, that will affect patients. So, we want a system that not only pays appropriately but makes the drugs available for treatment appropriately. If risk adjustment is the problem, why would we want to implement a bundled payment without having the ability to risk adjust it?

So, I do not differ on the goal at all. I am just a little mystified. I want to learn more about how we are going to achieve that goal, and I want to be sure that the knowledge base is firm before we make a national change in our National payment system. That is my only concern.

Chairman THOMAS. Will the gentlewoman yield in terms of that concern?

Ms. JOHNSON OF CONNECTICUT. Certainly.

Chairman THOMAS. Notwithstanding the obvious difficulty, given the time lag, does it make any sense at all in focusing on this that we could at least begin to nail down a couple of specifics that does not involve the universal concerns that are being discussed?

Number one, at what point do we begin to focus on the question of the percentage dosage? When you have got an FDA rate, you have got a label recommendation, you have got a manufacturer putting out a warning label, you have got studies that produce it, and you have CMS continuing to increase the percentage, at least that could be reconciled.

Secondly, if you have other drugs that could possibly provide or a structure in which when you do not have—and a lot of times what we have done is, when you do have a monopoly, you can create Government as a surrogate competitor and create a price which would control the amount, rather than leaving it to open market and incentives which are designed to require people to continue to use larger amounts.

Within the current structure, you have at least several, I would think, abilities to adjust payment arrangement competition and come to some agreement at least on the conservative do-less-harm side about the dosage question.

Could not we at least do those while they are trying to complement risk factors and other arrangements?

Mr. WALKER. We are saying similar things, Mr. Chairman, just in different ways.

The other thing I would suggest is, it seems to me that there is also a possibility to continue the demonstration project, move to some type of a bundled payment system with the consideration that there might be some adjustment in payment at some future date depending upon the results. But I would leave that to the CMS administrator.

Ms. JOHNSON OF CONNECTICUT. Reclaiming my time. Let me also put one other thing on your agenda, because I was not aware of that until this hearing. If you can titrate up to a stable dosage or if you can deliver this treatment more cheaply through injection, why are we not looking at those things, too? Because our bundled payment ought to take into account the lower cost of a different delivery system. Did you look at those issues?

Mr. WALKER. We did. One of the things that is included in our report is our point about the need for clinical flexibility to consider alternative means to be able to achieve the desired result, which includes what you said, Mrs. Johnson.

Ms. JOHNSON OF CONNECTICUT. We certainly do want that clinical flexibility if the patient is going to be served. That goes to the bundling issues and the risk.

Chairman THOMAS. Yes, obviously, if in fact another portion of the Government is using the subcutaneous method, you would at least think that that could be an option that you would look at, given the cost deferential.

The gentleman from California.

Mr. STARK. General Walker, thank you for this report.

You indicate that CMS has no procedure for validating the accuracy of the manufacturer's average sale price, which the manufacturer computes. I mean, they say, here is our average sales price, and we have no way to verify that, as I gather.

So, if I said what you are suggesting is that Amgen tells CMS what the average sales price is for Epo and then they go out and

sell it at whatever price they want to sell it, perhaps there are deep discounts to volume purchasers.

Do we know? Is that transparent to you? Do you know, are there big discounts? Do we have any idea how this pricing system works?

Mr. WALKER. Mr. Stark, we know what the statute says. The administrator may want to address what, if any, concerns they have about what they can do, given the statutory language. But what we can tell you is this, is we do not think there is adequate transparency and we don't think there is adequate work being done to verify the average sales price.

I reflect back—I am a Ronald Reagan, George Herbert Walker Bush and Bill Clinton Presidential appointee. We can all remember President Reagan saying: Trust but verify. That applies to drug prices, too.

Mr. STARK. Thank you very much.

Chairman THOMAS. We have been discussing bundling in terms of the Government's ability to create a structure which would limit controlling. It is my understanding that the private sector has had an ability to create bundling in terms of the purchase of drugs that are used. Is that—did you examine that at all, the way in which the provider, the manufacturer of the drugs is bundling the use of particular drugs as an incentive?

Mr. WALKER. We did not look at that in the context of this report.

Chairman THOMAS. Are you aware of it?

Mr. WALKER. Somewhat, yes.

Chairman THOMAS. We will ask that question.

Mr. WALKER. There is unbundling that occurs, too, in order to affect pricing.

Chairman THOMAS. Absolutely. So, bundling is on both sides.

Any additional questions? Thank you very much, and I apologize for causing you some problem in trying to get across the bridge.

Mr. WALKER. Thank you, Mr. Chairman.

Ms. TUBBS JONES. Mr. Chairman, I want to introduce something for the record. Mr. Chairman, thank you very much for the opportunity.

Mr. Walker, I want to introduce for the record two articles by a constituent of mine by the name of Dr. Wish. Dr. Wish is a physician at University Hospital in Cleveland; and, in that capacity, he is a Professor of Medicine and the Medical Director of Hemodialysis Services at University Hospital.

Among other things, Dr. Wish is the President of the End-Stage Renal Disease Network, and he is on the CMS Advisory Board, and he asked me to specifically introduce into the record two of his articles: One of them, The Economic Realities of Erythropoiesis-Stimulating Agent Therapy in Kidney Disease, and another one, an editorial, Can Evidence Drive the Development of a Sound National Epo Reimbursement Policy for the United States?

I am assuming you know Dr. Wish and his prominence in this area. I thought as long as we were discussing these issues it would be important that we have some information from his background into the record.

Mr. Chairman, I thank you very much for the opportunity.

Chairman THOMAS. Thank you very much.

Thank you, Mr. Walker.
[The information follows:]

EDITORIAL

Can Evidence Drive the Development of a Sound National EPO Reimbursement Policy?

Related Article, p. 111

THE CURRENT Medicare epoetin (EPO) reimbursement policy for end-stage renal disease (ESRD) patients is broken and in need of repair.

THE QUALITY STORY

In 1993, the Health Care Financing Administration (HCFA; now known as the Centers for Medicare and Medicaid Services [CMS]) shifted the quality oversight model for the ESRD program from a quality assurance (QA) focus to a quality improvement (QI) focus as part of their more global Health Care Quality Improvement Program (HCQIP).[1] Two major components of the HCQIP for the ESRD program were the National Core Indicators Project and the National Anemia Cooperative Project. The National Core Indicators Project (which continues today as the ESRD Clinical Performance Measures Project) was designed to provide an annual "snapshot" of outcomes for hemodialysis and peritoneal dialysis patients in key areas of care. The National Anemia Cooperative Project was developed as a model for QI, given the significant opportunities for improvement in the management of anemia in dialysis patients that were identified in 1993, 4 years before the NKF/DOQI clinical practice guidelines for the treatment of anemia in patients with chronic kidney disease were published. In the fourth quarter of 1993, only 46% of hemodialysis patients in the Core Indicators random sample had a 3-month average hematocrit (Hct) greater than 30%.[2] The National Anemia Cooperative Project fostered the application of QI principles to anemia management by providing every dialysis facility with an anemia treatment algorithm developed by an "expert panel," facility-specific data regarding patient Hct and EPO doses based on Medicare billing records and generic QI tools. The National Anemia Cooperative Project was considered a success because between 1993 and 1997 (the year the NKF/DOQI anemia guidelines were published), the percentage of hemodialysis patients with Hct >30% consistently increased from 46% to 79%.[2]

Following the publication of the original set of NKF/DOQI clinical practice guidelines in 1997, HCFA contracted for the development of clinical performance measures derived from the guidelines, including those addressing anemia management. Since the NKF/DOQI anemia guideline recommends a target hemoglobin (Hgb) of 11 to 12 g/dL (110 to 120 g/L) for ESRD patients receiving EPO, the ESRD Clinical Performance Measures Project, successor to the National Core Indicators Project, has used Hgb ≥11 g/dL (110 g/L) as its reporting benchmark. Anemia data from the 5 years of the ESRD Clinical Performance Measures Project are shown in the Table 1.[3]

One of the fundamental concepts of continuous quality improvement (CQI), upon which the HCQIP is based, is that consistency of process will lead to consistency of outcomes. The widespread application of evidence-based practice guidelines, such as the NKF/DOQI anemia guidelines, has led to improved outcomes, as demonstrated by the annual increases in percentage of patients with Hgb ≥11g/dL (110 g/L) and mean Hgb, but has not led to a significant decrease in the variability (standard deviation [SD]) in Hgb. The random variation in a human laboratory test such as Hgb, which is affected by variability in dose responsiveness to administration of EPO and iron, by the state of patient hydration, by the reproducibility of the Hgb assay itself, and by biologic differences inherent in a diverse patient population, is likely to be much greater than the variation in the diameter of a product that is made by a standardized manufacturing process. The appropriate application of CQI principles, which were designed originally for manufacturing industries and applicable in many ways to

0272-6386/03/4101-0036$35.00/0
doi:10.1053/ajkd.2003.50067

Table 1. Anemia Data From the 5 Years of the ESRD Clinical Performance Measures Project

Year	% Patients With Hgb ≥11 g/dL	Mean Hgb (g/dL)	Hgb Standard Deviation	% Patients Prescribed EPO IV	Mean IV EPO Dose (units/kg/dose)	% Patients Prescribed Iron IV
1997	43	10.73	1.22	92	65.6	51
1998	59	11.14	1.26	89	69.0	57
1999	68	11.42	1.29	88	81.0	59
2000	74	11.63	1.23	88	82.6	64
2001	76	11.67	1.20	90	85.5	64

NOTE. Conversion factor: to convert Hgb to units of g/L, multiply by 10.0.

healthcare, cannot eliminate outcome variability that is a function of biologic diversity.

THE COST STORY

When Medicare first approved payment for EPO in ESRD patients in 1989, EPO administration was reimbursed at the flat rate of $40 per dose, irrespective of the amount of EPO administered. In 1991, the Medicare reimbursement rate for EPO was changed to $11 per 1,000 units. This change in reimbursement policy was followed by a rapid escalation in the average EPO dose, based on 3 times weekly administration, from 2,700 units to 4,200 units by mid 1993, but an increase in average hematocrit only from 28.8% to 29.6%.[4] With 46% of hemodialysis patients having Hct ≥30% in 1993,[3] "high" Hct or Hgb levels were not a major issue with EPO reimbursement policy. However, as the Hct distribution curve moved progressively to higher values between 1993 and 1996 due to the success of the National Anemia Cooperative Project and reimbursement policy that favored larger doses of EPO, the percentage of ESRD patients with Hct >36% inevitably grew. In 1996, the draft of the NKF/DOQI anemia guidelines was released for public comment. The draft included a guideline that the target Hct for ESRD patients treated with EPO should be 33% to 36%. The EPO reimbursement policy subsequently issued by the payment office at HCFA denied payment for patients whose 3-month rolling Hct exceeded 36% and rejected any allowance for reduction in the EPO dose in patients whose Hct exceeded the ceiling. Not unexpectedly, this reimbursement policy made ESRD providers very conservative in their EPO dosing for fear of exceeding the Hct ceiling and jeopardizing their EPO reimbursement. In 1997, only 43% of hemodialysis patients had a Hgb level that exceeded the lower target of 11 g/dL (110 g/L).[2]

In 1998, the HCFA issued a new EPO reimbursement policy that raised the 3-month rolling average Hct ceiling to 36.5%, prohibited prospective payment denial by fiscal intermediaries, and made an allowance for the reduction in EPO dose in response to a high Hct with full reimbursement for a 20% reduction in dose. Concurrent with the liberalized reimbursement policy was the expected shift in Hct distribution to higher values, although the rate of annual rise in percentage of patients with Hgb ≥11 g/dL (110 g/L) and mean Hgb has decreased between 2000 and 2001. This observation suggests that reimbursement concerns have become a limiting factor in the continued movement of the Hgb distribution curve, such that approximately 24% of hemodialysis patients will fail to achieve the NKF/DOQI target Hgb of 11 g/dL (110 g/L) on any point prevalence sample. The national coverage policy prohibiting prospective payment denial for EPO expired on September 15, 2001, but was reinstated on August 31, 2002. This reinstatement expires August 31, 2003. If the national coverage policy is again allowed to lapse, the default prospective payment denial for EPO by fiscal intermediaries may cause the Hgb distribution curve to shift back to lower values.

THE EVIDENCE

The study by Besarab et al[5] is frequently cited by CMS as evidence that ESRD patients with cardiac disease and, by extrapolation, all ESRD patients have worse outcomes when their anemia is treated to a target Hct of 42% as opposed to 30%. Also cited as a justification for the Hct reimbursement ceiling is a report based on Medicare billing data from 1993-1994[6] that concluded

that patients with Hct 33% to 36% had the lowest risk of cardiac and all-cause mortality, but that excluded patients with Hct >36% from the mortality analysis because of their high comorbidity. However, subsequent analyses have demonstrated lower mortality,[7] decreased hospitalizations,[8] and better quality of life scores[9] in hemodialysis patients whose Hct is higher than the 33% to 36% NKF/DOQI target range. In June 2001, the Agency for Healthcare Research and Quality concluded that "the published literature does not provide strong or consistent support that maintaining Hct above 36 percent is more beneficial to patients with CRF than maintaining Hct in the target range of 33 to 36 percent as recommended by NKF/DOQI. Limited data on physiologic measures suggest a possible benefit for selected patients when Hct is maintained above 36 percent. However, the potential for benefit should be tested in well-designed intervention studies."[10]

Whether patients with Hgb >12 g/dL (120 g/L) have better outcomes than those with Hgb 11 to 12 g/dL (110-120 g/L) is not the issue regarding the EPO reimbursement ceiling; the issue is that the Gaussian distribution of Hgb values in the ESRD population is such that a large percentage of patients will inevitably have Hgb >12 g/dL (120 g/L) if a desirable percentage have Hgb >11g/dL (110 g/L). It is that truth which must be recognized in a rational Medicare EPO reimbursement policy for ESRD patients.

THE BOTTOM LINE

Given the compelling evidence that Hgb levels <11 g/dL (110 g/L) are associated with poorer outcomes and the inconsistency of evidence that Hgb levels >12 g/dL (120 g/L) are associated with better or worse outcomes than Hgb levels between 11 and 12 g/dL (110 to 120 g/L), it would seem that a Medicare EPO reimbursement policy that does not promote the maximum number of patients achieving a Hgb ≥11 g/dL (110 g/L) is not in the best interest of Medicare beneficiaries. The data presented by Lacson et al[11] in this issue of the *Journal* elegantly demonstrate that, despite consistent application of the NKF/DOQI anemia treatment guidelines in a large dialysis chain, the width of the Hgb distribution curve did not change over a 6-year period due to significant intrapatient variability (median Hgb SD, 0.7 g/dL [7 g/L]) as well as interpatient variability that represents biologic diversity. Furthermore, as shown by Fig 2 in the article by Lacson et al,[11] there is a continuous shift of patients among groups at, above, and below the Hgb target range from quarter to quarter in the representative year. This intrapatient variability means that a 3-month rolling average Hgb for an individual patient may still have sufficient "noise" to make it unsuitable for use as an EPO reimbursement trigger, and that the use of a longer Hgb averaging period, such as 6 months, should be considered for EPO reimbursement purposes. This approach reduces the SD of Hgb measurement from 1.18 to 0.99. If a reasonable goal is to have 85% of hemodialysis patients with Hgb ≥11 g/dL (110 g/L), then based on the Hgb distribution characteristics reported by Lacson et al,[11] 63% of patients must have Hgb >12 g/dL (120 g/L) and 32% of patients must have Hgb >13 g/dL (130 g/L) (Table 2 in the article by Lacson et al[11]). This scenario is clearly incompatible with the current Medicare EPO reimbursement policy.

The data reported by Lacson et al[11] were from a single dialysis chain, and one could question whether the anemia management policies in that chain might themselves have posed a barrier to decreasing intrapatient and interpatient Hgb variability. However, Brier and Aronoff[12] report similar results and conclude that the current Hgb target range is unrealistically narrow and should be liberalized.

If Medicare EPO reimbursement policy were liberalized to recognize a wider target range for Hgb based on the inevitable Gaussian ESRD population distribution in the setting of appropriate anemia management practices, then how should such a revised policy be financed? One possibility would be to capitate EPO reimbursement at a fixed level. This approach would remove any Hct or Hgb reimbursement ceiling and allow providers to tailor EPO management to individual patients' needs. The funding would be determined by calculating the current average EPO dose for ESRD patients (90% of which is administered IV) and capitating at that level. A multivariate regression model of patient demographic and comorbidity information versus EPO reimbursements reported by the Kidney Epidemiology and Cost Center[13] found that the only

identifiable patient characteristics that had a statistically significant impact were patient weight, age, and presence of HIV/AIDS. Consequently, a capitated EPO reimbursement policy could easily be adjusted for these case-mix factors. Under a capitated EPO reimbursement policy, EPO would shift from being a profit center to a cost center for dialysis providers, providing an incentive to conserve EPO by administering it subcutaneously (SC) rather than intravenously (IV), as already done in most of Europe, where the mean weekly EPO dose for hemodialysis patients in 2000 was 62% below that in the United States (92 U/kg/wk in Europe versus 243 U/kg/wk in the United States).[14] A meta-analysis of SC versus IV EPO in hemodialysis patients reported by Besarab et al[15] showed a more modest 48 U/kg/wk reduction in EPO dose in patients treated with SC versus IV EPO that translated into an annual average cost savings of $1,761 ± $1,080 (SD) per patient. Under a capitated EPO reimbursement system, these annual cost savings would be retained by the dialysis facility to support other patient care services, addressing the concerns by Meyer and Kassirer[16] that the lower profitability of SC EPO administration would cause patient care to suffer because most dialysis providers depend on the profit margin of EPO in the setting of the razor-thin margin (or loss) from the dialysis composite payment rate. Meyer and Kassirer[16] are also concerned that bundling EPO reimbursement into the composite rate would "cause human resources to bleed slowly into the erythron," but case-mix stratification of payment such as for weight, age, and presence of HIV/AIDS should lessen such concerns.

How would capitation of EPO reimbursement prove to be a more successful approach to anemia management than it was in 1990? First, there are evidence-based practice guidelines for the treatment of anemia in patients with renal disease with recommendations regarding target Hgb level and iron management that did not exist in 1990. Second, outcome studies have demonstrated the benefits of achieving the target Hgb of 11 to 12 g/dL (120 g/L) in terms of decreased mortality and hospitalizations. Therefore, it is in the best interest of dialysis providers as well as patients to maintain these Hgb levels so that the patients stay alive and out of the hospital. Third, there is more accountability for outcomes by dialysis providers than there was in 1990 through the ESRD Networks, State surveyor agencies, and the public Dialysis Facility Compare website. Over the next 1 to 2 years, clinical performance measures data, including anemia management, will be collected electronically from dialysis facilities and dialysis chains on a 100% patient sample in real time so that the information for quality oversight and public accountability will be current and more actionable.

The data presented by Lacson et al[11] and by Brier and Aronoff[12] demonstrate that the current Medicare approach to EPO reimbursement for ESRD patients is flawed. The lapse of a national reimbursement policy allowed fiscal intermediaries to prospectively deny EPO reimbursement to providers, which can jeopardize the quality of patient care. The current 3-month rolling average Hct/Hgb reimbursement ceiling fails to acknowledge the width of the Hgb distribution curve and is a barrier to a greater percentage of patients achieving a Hgb ≥11g/dL (110 g/L). The thin margin of the dialysis composite rate forces providers to depend on separately billable drugs such as EPO to stay in business, resulting in the vast majority of patients receiving EPO IV when much smaller doses administered SC would be as effective. This approach has led to a questioning of the responsibility and credibility of American nephrologists by a Canadian counterpart.[17] CMS is currently considering a revised prospective payment system for dialysis and will be conducting a demonstration project in the near future. It is hoped that the new system will provide the appropriate incentives and decrease the barriers to optimal management of anemia in the context of improving the overall care for ESRD patients.

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The economic realities of erythropoiesis-stimulating agent therapy in kidney disease

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The administration of erythropoiesis-stimulating agents (ESAs) in the United States provides a classic example of how economics drive practice. When epoetin was first approved for the treatment of anemia in 1989, its use in hemodialysis patients was very conservative as long as it was reimbursed at a single capitated rate of $40 irrespective of dose. Once epoetin was reimbursed at a rate of $11 per 1000 U in 1991, its use skyrocketed. Despite two iterations of clinical practice guidelines recommending subcutaneous (SC) over intravenous (IV) epoetin administration in hemodialysis patients based on ample evidence that the former is significantly more effective, 95% of hemodialysis patients in the United States receive epoetin IV because epoetin is a profit center for dialysis providers and Medicare has been willing to pay for it. Although darbepoetin is about twice as expensive as epoetin for the same therapeutic effect in patients with chronic kidney disease, darbepoetin has achieved significant market penetration despite the higher cost burden for patients with co-pays and data demonstrating that comparable dosing intervals can be achieved in a majority of patients treated with epoetin. It is likely that increased attention to costs of medications by providers through reimbursement bundling models, payment for performance systems, and competition by newer therapeutic agents will have a significant impact on current practice patterns.

Kidney International (2006) **70**, S21–S25. doi:10.1038/sj.ki.5001972

KEYWORDS: erythropoiesis-stimulating agents; anemia; economics; reimbursement; medicare

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The influence of economic realities on the erythropoiesis-stimulating agent (ESA) therapy for patients with kidney disease in the United States is undeniable. The most graphic demonstration of this phenomenon is illustrated in Figure 1.[1] Note that during the first year or so after epoetin was first released for use in hemodialysis patients, it was capitated at $40.00 per dose, irrespective of the number of units administered. As a result, use of the medication was quite conservative, averaging approximately 2700 U per patient three times weekly for the entire period. At the beginning of 1991, Medicare changed reimbursement policy for epoetin to $11.00 per 1000 U. This was followed by a rapid escalation of epoetin dosing over the next 3 years, which averaged approximately 4200 U per patient three times weekly by mid-1993.

ESAs IN HEMODIALYSIS

The Medicare reimbursement rate for epoetin was subsequently reduced to $10.00 per 1000 U for hemodialysis patients. Nonetheless, most hemodialysis providers could purchase epoetin for considerably less than this reimbursement rate, making epoetin a considerable profit center for dialysis providers in the United States. Therefore, the more epoetin dialysis providers administered, the more money they made. Despite the publication of the first set of clinical practice guidelines for the treatment of anemia in patients chronic kidney disease (CKD) by the National Kidney Foundation's Dialysis Outcomes Quality Initiative in 1997 which recommended the subcutaneous (SC) administration of epoetin in hemodialysis patients,[2] in 2004 only 5% of hemodialysis patients in the United States received their epoetin subcutaneously[3] as opposed to greater than 90% in Europe.[4] The revised clinical practice guidelines for the treatment of anemia in patients with CKD published by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative in 2001[5] also recommended that epoetin be administered SC to hemodialysis patients. Multiple studies and meta-analyses have shown that epoetin is 20–30% more effective when given SC versus intravenously (IV) with an annual cost savings of $1761 ± $1080 per patient.[6] In 2004, the mean weekly epoetin dose for hemodialysis patients in the United States was 150 U/kg when administered SC versus 198 U/kg when administered IV.[3]

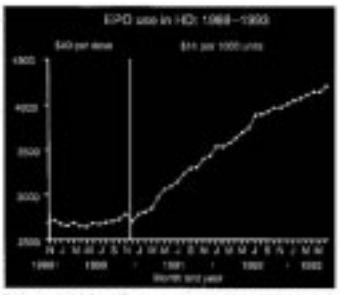


Figure 1 | EPO use in HD: 1989–1993.[1]

So the question arises why dialysis providers in the United States have resisted the recommendations of two iterations of clinical practice guidelines and the standard of care in other parts of the world by continuing to administer epoetin IV in 95% of hemodialysis patients. A number of rationalizations have been offered, including the fact that hemodialysis patients would prefer to avoid the sting of SC injections by receiving the medication IV and that SC erythropoietin carries a risk of pure red cell aplasia, but the reality is that dialysis providers in the United States administer epoetin IV because it makes them more money. Most dialysis providers have an extremely thin margin or actually lose money on the dialysis procedure itself, so they depend upon the profits from separately billable medications such as epoetin to stay in business. Thamer *et al.*[7] demonstrated that although mean hematocrit was not significantly different based on route of administration (34.4% for SC and 34.5% for IV users), the average weekly dose of epoetin was 14 143 U for SC users and 17 956 for IV users. Furthermore, patients were statistically significantly more likely to receive IV epoetin if they were treated in a freestanding for-profit dialysis facility, in a large non-chain facility, if the facility received greater than 11% of its payments attributable to injectables other than epoetin, if the patient resided in the Northeast part of the United States, and if the patient was dialyzed using a catheter. Although it may be difficult to explain the independent regional variation in IV epoetin administration, it is not difficult to suggest that the largest for-profit dialysis chains and non-chain facilities, accountable to their stockholders and Wall Street analysts, are more likely to augment their bottom line by increasing their epoetin use through IV administration. The economic irresponsibility related to the widespread use of IV epoetin in the United States has led to the public questioning of the responsibility and credibility of American nephrologists by a Canadian counterpart.[8]

Understanding the perverse economic incentives that have resulted from the profitability of separately injectable drugs and the unprofitability of the composite rate for hemodialysis treatments in the United States, Medicare in 2005 changed its policy to reimburse separately billable drugs in dialysis at a much less profitable average selling price (ASP) plus 6%, and to add the profit margin that was previously attributable to separately billable drugs to the dialysis composite payment so that total expenditures would be budget neutral. In 2006, this drug profit margin component increased the dialysis composite rate by 14.5%. Although this policy change may be a step in the right direction to economically discourage the excessive use of injectable drugs in dialysis patients, the ASP plus 6% reimbursement rate for epoetin will still make the drug profitable for most providers, encouraging the use of larger doses by IV administration. Eventually, after the completion of a demonstration project, all injectable drugs administered in the hemodialysis unit will be bundled into a case mix adjusted composite rate, at which time these medications will become a cost center rather than a profit center for the provider. At that time, at least two competitors to epoetin, darbepoetin and continuous erythropoietin receptor activator, may have made significant penetration into the hemodialysis market. Both of these newer agents are equally effective when administered IV or SC. As there is no dosing penalty for these newer agents when administered IV, it is likely that IV administration will predominate in the hemodialysis environment irrespective of a bundled composite payment. However, for providers continuing to use epoetin in a bundled payment environment, the dosing penalty of IV administration will inevitably drive an increase in SC use.

On 1 April 2006, Medicare changed its reimbursement policy for ESAs administered to hemodialysis patients. Any ESA claim for a patient with a hematocrit greater than 39% (hemoglobin greater than 13 g/dl) should have a dose reduction of 25% which would be noted using a modifier G8 code. ESA claims for patients with a hematocrit greater than 39% without this modifier will have the payment reduced by 25%. This 25% reduction in Medicare payment for ESA administration is based on a month-to-month change in total ESA administered, not a treatment-to-treatment change before and after the dosage reduction has occurred. Therefore, many providers are waiting until the end of the calendar month to reduce the ESA dose in patients with a hematocrit greater than 39%, even though a hematocrit value earlier in the month would have otherwise triggered such a dose titration according the facility's own protocol. This practice results in the excessive use and cost for the ESA during the balance of the month when a dosage reduction might have otherwise occurred, and may increase the potential risks to the patient that are attributable to an elevated hematocrit level.

Another provision of the 1 April 2006 change in Medicare ESA reimbursement policy is that any dose of epoetin greater than 500 000 U or darbepoetin greater than 1500 mcg per month will not be paid at all as this is a 'medically unbelievable error'. The ASP for epoetin in the first quarter of 2006 was $9.027 per 1000 U. Therefore, at the reimbursement

ceiling, 500 000 U would cost $4513. The ASP for darbepoetin in the first quarter of 2006 was $2.989 per mcg. Therefore, 1500 mcg would cost $4483. Although these two doses are comparable in cost, they are not comparable in efficacy. If one assumes, based on a review of the relevant literature, that there is approximately a 250:1 potency ratio for a unit of IV epoetin versus a (mcg) of darbepoetin, 375 000 U of epoetin would have the same potency as 1500 mcg of darbepoetin. The conclusion is that ESA-resistant patients can receive more effect from epoetin than from darbepoetin under the current reimbursement ceiling.

ESAs IN CKD

As noted above, the major economic issue for epoetin therapy in hemodialysis patients is SC versus IV administration. This is not an issue for patients with CKD as virtually all will receive their ESA SC. In patients with CKD, the major economic issue is the choice of the ESA, epoetin versus darbepoetin.

Despite increasing recognition of the prevalence and adverse physiologic consequences of anemia among patients with CKD, data from the end-stage renal disease (ESRD) Medical Evidence Report (Centers for Medicare and Medicaid Services form 2728) reveal a relatively flat penetration of ESA therapy among incident ESRD patients in Networks 9 and 10 (OH, KY, IN, and IL, Table 1). In 2005, only 29% of incident ESRD patients in Networks 9 and 10 received an ESA before initiating renal replacement therapy despite a mean hemoglobin of 10.36 g/dl. Figure 2, from the 2004 USRDS Annual Data Report,[9] shows that the data for Networks 9 and 10 are fairly representative for the United States at large, with some geographic variation. Nonetheless, data from a 100-nephrologist survey performed by BioTrends Research Group Inc., an independent consulting company which has gauged ESA use trends in CKD (personal communication, accessible at www.bio-trends.com), shows that these nephrologists were treating 74.6% of their stage 5 CKD patients and 52.3% of their stage 4 CKD patients with ESAs (Figure 3). This discrepancy with the Network 9–10 and USRDS data suggests that either these surveyed nephrologists are overestimating their ESA use in their CKD patients and/or a significant percentage of incident ESRD patients never have the opportunity to receive ESA therapy because they were not treated by a nephrologist before their requiring renal replacement therapy.

Table 2 summarizes data from Medstat Market Scan and Medicare Research databases between 2000 and 2005 for outpatient ESA prescriptions among patients with CKD-related anemia.[10,11] The percentage of patients in each dosing interval category does not add up to 100% because many patients received ESA doses at more than one interval during the observation period. The most common dosing interval for epoetin was ≤q1 week and the most common dosing interval for darbepoetin was q2 weeks. Irrespective of the dosing interval, the epoetin to darbepoetin dosing ratio was approximately 200:1.

Table 3 summarizes epoetin and darbepoetin dosing patterns in three large managed care organizations from the fourth quarter of 2001 through the third quarter of 2004.[12] Although significantly more patients treated with darbepoetin receive their medication at q2 week or ≥q3 week dosing intervals than those receiving epoetin, the average weekly cost for the darbepoetin was $241 as compared to $100 for

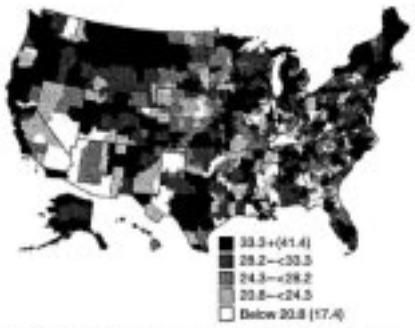
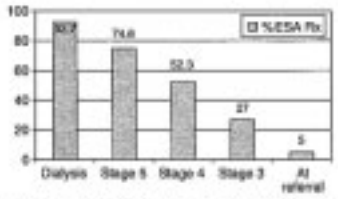


Figure 2 | Treatment of CKD patients with epoetin varies across the United States (2001–2002).[9]

Table 1 | Incident dialysis patients in OH, IN, KY, and IL (ESRD Medical Evidence Report)

Year	Total forms	Mean Hb	% All pts on EPO	% Pts Hb <10 on EPO
1998	9213	9.94	25.1	22.4
1999	10 211	10.14	26.5	23.6
2000	11 507	10.47	28.8	25.8
2001	10 760	10.64	30.5	26.5
2002	11 508	10.93	29.7	26.7
2003	13 075	10.48	29.3	26.0
2004	12 867	10.11	29.1	24.9
2005	11 969	10.36	29.5	25.0

EPO, epoetin; ESRD, end-stage renal disease; Hb, hemoglobin; IL, Illinois; IN, Indiana (subs); KY, Kentucky; OH, Ohio; pts, patients.



Survey of 100 nephrologists by BioTrends Research Group Inc. Personal communication.

Figure 3 | Prevalence of ESA Therapy by Stage of CKD.

Table 2 | MedStat Market Scan and Medicare Research databases 2000–2005[10,11]

	Epoetin (n=32408)		Darbepoetin (n=1286)		
Dosing interval	% Patients	Avg. weekly dose (U)	% Patients	Avg. weekly dose (U)	Epoetin to darbepoetin ratio
≤q1 wk	49	17198	9	83	207
q2 wks	19	9371	43	47	199
q3 wks	2	7851	5	34	231
Q4 wks	4	7568	7	25	302
≥q4 wks	3	6412	9	27	237

wk, week.

Table 3 | Three large managed care organizations 4Q2001–3Q2004[12]

	Epoetin (E)	Darbepoetin (D)	Ratio
Dosing Frequency			
q1 wk	23.4%	5.5%	
q2 wks	34.8%	46%	
≥q3 wks	26.6%	44.5%	
Avg. weekly dose	8165 U	57 mcg	149 (E:D)
Avg. weekly cost	$180	$241	2.41 (D:E)

wk, week.

epoetin, and the dosing ratio was 149:1 epoetin unit to darbepoetin mcg.

Monzale *et al.*[13], in a pharmaco-economic review for the Department of Veterans Affairs, analyzed the nephrology literature addressing the use of ESAs in patients with CKD, addressing study designs, dosing regimens, patient entry criteria, study end points, and cost data. These authors found that the average cost of epoetin during the first year predialysis was $3000, as compared to an average cost of darbepoetin during the first year predialysis of $7000, for a cost ratio of 2.33:1, darbepoetin to epoetin, making epoetin the better pharmacoeconomic value of the two currently available ESAs. Although a similar analysis has not been done by the Agency for Healthcare Research and Quality for patients with CKD, the Agency for Healthcare Research and Quality found that epoetin and darbepoetin have similar efficacy, complication rates, and quality of life measures when used to treat cancer patients.[14]

As noted above, the ASP for epoetin in the first quarter of 2006 was $9.027 per 1000 U and the ASP for darbepoetin was $2.989 per mcg. If one assumes a 200:1 SC epoetin to darbepoetin dosing ratio with an average EPO dose of 20 000 U q2 weeks and an average darbepoetin dose of 100 mcg q2 weeks, the cost of each dose of epoetin would be $184.54 and each dose of darbepoetin would be $298.90, for a cost ratio of 1.66:1 darbepoetin to epoetin for Medicare patients.

So why would one choose to administer the more expensive darbepoetin versus epoetin in patients with CKD-associated anemia? Is it worth it for patient convenience associated with the longer dosing interval for darbepoetin even though darbepoetin costs approximately twice as much as epoetin for the same therapeutic effect? Data from the PROMPT study[15] suggest that epoetin is effective in achieving target hemoglobin ⩾11.0 g/dl in 76% of CKD patients when administered as infrequently as q4 weeks. This further calls into question whether the dosing interval advantage of darbepoetin can justify its considerably higher cost. As ESAs are reimbursed by Medicare at ASP plus 6%, the 6% of darbepoetin's greater ASP would yield the provider a larger potential profit margin than 6% of the lower ASP for epoetin. However, as most patients have a co-pay for their pharmaceuticals, which in the case of Medicare beneficiaries is 20% on ESAs covered under Part B, the yearly patient co-pay for epoetin administered in a typical dose of 20 000 U q2 weeks would be $939. The yearly co-pay for a therapeutically equivalent dose of darbepoetin, administered at 100 mcg q2 weeks, 150 mcg q3 weeks, or 200 mcg q4 weeks would be $1554. This additional financial burden on a typical patient with CKD is not insignificant, and should give the provider cause to consider whether it can be justified.

SUMMARY

The unfortunate but inevitable conclusion from 27 years experience with ESAs in the United States is that misaligned economic incentives in a fee-for-service system may result in therapeutic choices that favor provider reimbursement. Perhaps the overall unfavorable economic climate for health care providers has forced many into making these decisions to stay in business. Nonetheless, considerable system-wide savings could be achieved by using SC rather than IV epoetin in in-center hemodialysis patients and by using epoetin rather than darbepoetin in patients with CKD not yet on dialysis. The bundling of injectable drugs with the dialysis composite rate, as it converts these agents from a profit center to a cost center, will inevitably drive an increased rate of SC administration as providers rein in expenditures. The implementation of payment for performance models in both the CKD and ESRD environments, which will likely include measures of cost conservation, will also impact on the choice of ESA and its route of administration. Finally, the availability of newer ESAs over the next several years will increase competition in the marketplace, driving the costs of these agents down, and providing additional choices to providers, patients, and payers.

ACKNOWLEDGMENTS

Conflict of interest statement: Advisory board - Ortho Biotech, Roche, Watson, Amgen; Speaker's Bureau - Ortho Biotech, Watson; Consultant - Roche.

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Chairman THOMAS. Let me say at the outset, any written testimony you have will be made part of the record. Ms. Norwalk, notwithstanding the fact that you are sitting here now as someone who is newly arrived in the position, filling a slot from someone who had been the head of the FDA and was a medical doctor, we are completely aware of the fact that these policies and decisions were ongoing and that for us to ask you with the expectation or be-

lief that you might be able to respond in depth, not saying that as you spend some time in that position you would not be able to but that at the onset and given the timing that we have, I want to encourage you, if we move into a questioning session, to feel perfectly comfortable asking any person who is part of the CMS support structure to identify themselves and come to the table so that you do not have to turn around and ask them the question and have them provide you the answer. Because that is a perfectly legitimate and proper way to operate, given how long you have been on the ground even in an acting capacity.

Ms. NORWALK. Thank you, Mr. Chairman.

Chairman THOMAS. It is not personal, and it is not directed toward you. You just happen to have currently moved very briefly into a position in which we expect you to know everything about everything, and that is not fair.

So, with that, the time is yours.

STATEMENT OF LESLIE V. NORWALK, ESQ., ACTING ADMINISTRATOR, CENTERS FOR MEDICARE AND MEDICAID SERVICES

Ms. NORWALK. Thank you, Chairman Thomas, distinguished Members of the Committee. Thank you for the opportunity to appear before you today.

Mr. Chairman, I also would like to wish you a happy birthday. As the Acting Administrator of CMS, this has special meaning in my heart, given that you are now an official Medicare beneficiary, entitled to all of the benefits that you helped create and improve during your service in Congress.

You asked me to be here today to discuss a very important issue, safety and quality in the treatment of patients with End-Stage Renal Disease, or ESRD. Roughly 400,000 Americans suffer from ESRD and are entitled to Medicare coverage on the basis of that diagnosis, regardless of age or disability.

The ESRD population has grown steadily in recent years. Although better management of diabetes and hypertension could help stem the growth, initiatives to promote efficient, high-quality ESRD care are integral to CMS's overall agenda and value-based payment reforms.

This administration has demonstrated a strong commitment to promoting quality across the board. CMS launched the Medicare Quality Initiative in 2001, promoting greater accountability in consumer choice through unprecedented public disclosure of provider performance on a range of quality measures.

To date, CMS has implemented initiatives focused on nursing homes, home health agencies, hospitals and dialysis facilities. We announced the ESRD Quality Initiative in 2004 to stimulate and support improving quality of dialysis care. For these and other efforts CMS was recognized earlier this year by the American Association of Kidney Patients for dedication to improving lives of kidney patients and strong leadership in health care for all Americans.

Projects such as Dialysis Facility Compare on the Web site and the Fistula First Breakthrough Initiative are just two examples of

the many steps CMS has taken to promote high-quality care for people with ESRD.

The Fistula First Breakthrough Initiative aims to increase the use of fistulas in hemodialysis treatment of patients with ESRD. Fistulas are considered to be the gold standard for establishing access to a patient's circulatory system as is required during hemodialysis.

Fistulas last longer, require less rework and repair and are often associated with lower rates of infection, hospitalization and death. Simply put, appropriate use of fistulas optimizes patient care, including a possible reduction in Epo dosing.

CMS also contracts with the End-Stage Renal Disease Networks across the country to help monitor and improve the quality of care for ESRD patients. The ESRD Networks are similar to the QIOs, which work with hospitals, physicians and other Medicare providers to promote quality and best practices.

Our networks focus on quality treatment, quality improvement and promoting transparency in renal dialysis treatment. Their efforts are complemented by our survey and certification process for ESRD facilities, which enforces compliance with regulations prescribing minimum standards for Medicare-approved dialysis facilities with respect to quality, patient safety and access to Medicare benefits.

I know that many of you share my strong interest in a more rational payment system for ESRD care, requiring a CMS report to Congress and demonstration under the Medicare Modernization Act of 2003 to advance a fully bundled ESRD prospective payment system. As you know, the GAO recently reported that such a payment structure would promote quality, safety and savings in the ESRD benefit; and I want to be clear that I completely agree.

While the MMA-required report is now overdue, I want to assure you that CMS is fully committed to completing the analytical groundwork relevant to a fully bundled payment system. CMS completed an initial round of research in mid-2006, but developing a payment model that adequately captured variation of dosage of Epo was a key, but difficult, area of this research. CMS felt that the approach examined in the initial round too closely linked the payment to actual drug utilization and so began a new phase of research to address this and other areas of our new payment structure.

Our current research, which is nearing completion, focuses on predictors used in the current basic system augmented by other adjusters such as comorbid conditions and other patient characteristics. I expect to receive the research findings from our contractor early next year and hope to detail those findings in our official report to you by next summer.

With the benefit of those findings and recent work of the GAO, MEDPAC and others, I look forward to working with you to develop an effective bundling proposal. I believe that payment reform is critical to improving ESRD patient care.

Finally, I have heard recently from you, Mr. Chairman, and from you, Mr. Stark, regarding a monitoring policy that we have in place to encourage appropriate use of anti-anemia agents in the ESRD population. Anemia can be severe and debilitating in ESRD pa-

tients if left untreated, but, fortunately, drug compounds with Epo in this context can largely alleviate the symptoms.

Anemia's severity is monitored by a patient's hematocrit, the proportion of red blood cells in whole blood. Scientific evidence and, indeed, FDA labeling for Epo indicate that patient hematocrit should be maintained between 33 and 36 percent for optimal results.

In a recent letter, you noted that CMS's hematocrit monitoring policy does not reduce provider payment for Epo until a patient's hematocrit reaches 39 percent. While this is accurate, we believe it is important to keep in mind the distinction between regulating the safety and effectiveness of a particular drug versus determining the amount a provider should be paid for administering that drug to a patient.

Our provider and contractor manuals specifically require providers to target a hematocrit range of 30 to 36 percent consistent with the FDA label. Moreover, we require that patient records reflect the clinical reason for dose changes and hematocrit levels outside of the 30 to 36 percent range.

Medicare contractors currently may review medical records to ensure appropriate dose reductions are applied and maintained and hematological target ranges are maintained. Hematocrit levels can change unexpectedly for a multitude of reasons. Our instructions to carriers about reviewing claims takes this into account.

Our monitoring policy for carriers is not establishing a therapeutic hematocrit target, which we believe is a clinical judgment appropriately left to a treating physician. Our monitoring threshold for carriers is slightly above the FDA label to avoid penalizing providers that make appropriate dose reductions in response to unexpected increases in their patients' hematocrit levels. Rather, 39 percent is a marker of the point at which a Medicare carrier must reduce payment to a provider because the reported hematocrit was not maintained at a level consistent with the FDA label. CMS developed this policy after considering the body of available scientific evidence as well as public comments received in response to our proposed policy issued in 2004.

We are, of course, very interested in recent research findings regarding Epo use in patients with chronic kidney disease. Following publication, a study of this nature typically is subject to international scrutiny and examination. Experts will review the study design, methodology results and conclusions. In fact, it would be very useful for CMS to have access to the raw data behind the CHOIR and other similar studies so we may take them into account as we continue to review our policies.

We look forward to further research developments on this issue. Like Congress, we are concerned about overuse and improper use of any drug we cover. We are always reassessing our policies to see if we can strengthen our programs to ensure the best possible patient outcomes.

I would be happy to answer any questions you may have.

[The prepared statement of Ms. Norwalk follows:]

Statement of Leslie V. Norwalk, Acting Administrator, Centers for Medicare and Medicaid Services

Chairman Thomas, Representative Rangel, thank you for the opportunity to appear before you today regarding important safety and quality issues in the treat-

ment of Medicare patients with kidney failure, or End Stage Renal Disease (ESRD). Roughly 400,000 Americans suffer from ESRD and require either kidney dialysis or transplantation to live. ESRD is Medicare's only disease-specific program; it entitles people of all ages to Medicare coverage on the basis of their ESRD diagnosis. The number of individuals covered under Medicare by virtue of their ESRD diagnosis continues to grow steadily. Estimates suggest that as many as 20 million Americans currently are afflicted by some stage of Chronic Kidney Disease (CKD). Many will progress to ESRD and the need for some form of renal replacement therapy unless new ways of treating CKD are found.

The Centers for Medicare and Medicaid Services (CMS) believes that in general, treatment decisions for ESRD patients are best left to the clinical judgment of treating physicians. The CMS is charged with determining appropriate coverage and payment for services to Medicare beneficiaries. In recent years, CMS has worked hard to ensure its coverage and payment policies promote high quality care, which is in the best interests of the beneficiaries we serve as well as the long-term financial health of the Medicare program.

Quality and safety initiatives have been at the center of the Administration's health care agenda for more than five years. We have made significant strides in promoting greater transparency in the health care industry, giving Medicare beneficiaries and all consumers unprecedented access to information that supports meaningful choices. Whether considering dialysis facilities, hospital services, skilled nursing providers or prescription drug benefits, people with Medicare can find the information they need to identify the best quality and value among available options. The CMS has devoted significant resources to ESRD quality and patient safety issues, with a comprehensive Quality Roadmap, the ESRD Quality Initiative, and ongoing research to explore ESRD payment reforms, among other efforts.

The Congress also has been an important partner in these achievements. Efforts such as the Care Management for High Cost Beneficiaries Demonstration create a platform for research to improve quality care and reduce the costs of caring for fee-for-service beneficiaries with one or more chronic diseases, who generally incur high Medicare costs. CMS has selected six sites under the demonstration, including one in New York state that focuses on beneficiaries with chronic kidney disease. Programs under the demonstration are testing ways to increase adherence to evidence-based care, reduce unnecessary hospital stays and emergency room visits, and help participants avoid costly and debilitating complications.

The CMS Quality Roadmap & Medicare's ESRD Quality Agenda

In 2005, CMS issued the "CMS Quality Roadmap," to promote the right care for every person, every time. The Quality Roadmap builds on the Institute of Medicine's six aims for healthcare: Patient-centered; Safe; Accessible; Effective; Efficient; and Equitable.

The CMS Quality Roadmap presents five strategies to achieve its vision:

- Partnering and collaborating with other healthcare stakeholders;
- Collecting and publicly reporting data that measures the quality, efficiency and cost of healthcare;
- Striving to reform healthcare reimbursement systems to promote quality and efficiency, while avoiding unnecessary costs and complications;
- Promoting the use and availability of clinical information for providers and Medicare beneficiaries, particularly through the adoption of health information technology, to assist them in providing and receiving high-quality and efficient care; and,
- Promoting the use of evidence-based healthcare information, in clinical, coverage, and payment systems, ensuring that the latest treatments, medical devices and services are available to clinicians and their patients, while avoiding inappropriate or wasteful use of those treatments.

Significant work and leadership in clinical quality initiatives also preceded the adoption of the CMS Quality Roadmap. In 2001, the Administration launched the Medicare Quality Initiative in pursuit of quality health care through accountability and public disclosure not just for Medicare patients, but for all Americans. Following the implementation of specific initiatives focused on nursing homes, home health, and hospitals, CMS announced the ESRD Quality Initiative in 2004.

Specific objectives of the ESRD Quality Initiative, which focuses on dialysis facilities, reflect an array of goals to stimulate and support improvement in the quality of dialysis care:

- Refining and standardizing dialysis care measures, ESRD data definitions, and data transmission to support the needs of Medicare's ESRD program;

- Empowering patients and consumers by providing access to facility service and quality information;
- Providing quality improvement support to dialysis providers;
- Assuring compliance with conditions of coverage; and,
- Building strategic partnerships with patients, providers, professionals, and other stakeholders.

While all efforts under the ESRD Quality Initiative are significant, the Fistula First Breakthrough Initiative is particularly noteworthy. Under the initiative, facilities submit data to Medicare contractors charged with quality review of dialysis facilities ("ESRD Network Organizations") to facilitate a more coordinated approach to care. The initiative has led to a significant increase in the use of AV Fistulas in treating dialysis patients—a measure associated with considerable reductions in avoidable hospitalization and death for ESRD beneficiaries.

The ESRD Quality Initiative also supports the annual collection of Clinical Performance Measures (CPMs) for a random sample of dialysis patients nationwide. With these measures, CMS can identify and track opportunities for improvement in areas such as the adequacy of hemodialysis and peritoneal dialysis, anemia management, and vascular access management. The Quality Initiative also includes the Dialysis Facility Compare resource on www.medicare.gov, which contains quality information for all Medicare approved dialysis facilities in the United States. Patients and consumers are able to search and compare facilities on this site and choose a dialysis facility that best meets their needs.

In addition to various efforts under the ESRD Quality Initiative, CMS partners with states to conduct regulation and enforcement activities to ensure that dialysis facilities comply with federal safety and quality standards. Under this survey and certification program, CMS establishes standards for safe and effective operation of dialysis facilities; develops guidelines and procedures; provides training for surveyors; and coordinates state activities. Currently, dialysis facilities are surveyed roughly every 36 months. State survey agencies also will investigate specific complaints on an as needed basis, outside of the regular survey cycle.

Finally, nearly all patients with ESRD suffer from debilitating anemia. Much of this anemia can be managed through drug therapy. CMS has had a quality initiative for years to encourage appropriate management of anemia in ESRD patients, including an active monitoring policy for patients being treated with erythropoietin.

All of these examples demonstrate a commitment by the Administration and CMS to ensuring and improving high quality care for the ESRD population. We have made significant strides over the last 5 years, and will continue to work to increase the availability of consistent, standardized core data elements that promote greater transparency and better care outcomes for ESRD patients.

Anti-Anemia Agents Used in ESRD Patients

Two prescription drugs commonly are used for anemia management in patients with ESRD who are dialyzed in renal facilities: epoetin alfa (Epogen®) and darbepoetin alfa (Aranesp®). These products rely on erythropoietin to help control anemia. To promote appropriate usage, CMS has in place a monitoring policy that considers both hematocrit levels and erythropoietin dosage levels.[1]

Current kidney disease clinical guidelines, determined through national consensus processes by multiple ESRD experts and stakeholders, call for maintaining the hematocrit level of patients receiving erythropoietin within a narrow target range of 33–36 percent. Because many factors such as nutritional status, infection, and bleeding may cause the hematocrit to fluctuate, it is not easy to manage patients to this narrow range. Some patients might be above (or below) the target in one month, for example, but below (or above) it in others. If one superimposes frequent and significant changes in doses of anemia management drugs on these existing fluctuations, patient hematocrit fluctuations can become even more variable and difficult to interpret and manage, particularly within the narrow target range of 33–36 percent.

Promoting Appropriate Payment through Hematocrit Monitoring

ESRD treatment facilities submit claims to CMS monthly for erythropoietin, which is billed separately from other dialysis services. The claim form includes

[1] Anemia severity is monitored by measuring the hematocrit with a simple blood test that reveals the proportion of red blood cells in whole blood. The hematocrit result is expressed as a percentage. Alternatively, the hemoglobin concentration in whole blood may be used to monitor anemia. The numeric value of the hematocrit is generally three times the value of the hemoglobin measured simultaneously, though they are expressed using different units. Thus, for example, a hematocrit of 30 percent corresponds to a hemoglobin concentration of 10 g/dl.

fields where the facility must report the beneficiary's hematocrit test result. Commonly, a dialysis patient's hematocrit level is tested many times during a month.

CMS is committed to establishing and maintaining policies in all areas of the Medicare program that protect beneficiaries, promote efficient and appropriate use of medical interventions, and enable providers to render excellent care. The newly revised CMS monitoring policy for erythropoietin used in ESRD patients instructs providers on how to submit claims, and instructs CMS contractors on how to adjudicate the claim. Under the policy, Medicare expects a 25 percent reduction in the dosage of erythropoietin for patients whose hematocrit exceeds 39.0. If the dosage is not reduced, payment is made for the drugs as if the reduction occurred.

The new monitoring policy is not a national coverage determination, and thus it is not a determination of the reasonableness and necessity of using an anti-anemia agent to maintain hematocrit levels above 36 percent. The monitoring policy clearly articulates that providers should adhere to the FDA label instructions for erythropoietin, i.e, seeking to achieve a hematocrit of 30–36 percent. The instruction to carriers to initiate monitoring when the hematocrit reaches 39 percent is not a new hematocrit range policy, but instead establishes a marker of the point at which payment must be reduced because the reported hematocrit was not maintained at levels consistent with FDA labeling.

The value 39 percent is not a therapeutic hematocrit target, which CMS believes is appropriately left to a treating physicians' clinical judgment. Rather, it is the target to initiate reduction in payment, a function appropriate to the mission of CMS. To be clear, it recognizes the difficulty in the clinical setting of maintaining the hematocrit in the narrow clinical guideline range of 33–36 percent, and therefore does not immediately cut off payment for a single hematocrit value that fluctuates above this narrow range. However, it does set in motion a policy that will reduce reimbursement if the hematocrit level remains above 39 and the provider does not reduce erythropoietin dosage as FDA labeling and national clinical guidelines indicate.[2]

A provider submitting a claim for erythropoietin in an ESRD patient with a hematocrit above 39 may inform CMS that a dose reduction has occurred, despite the continued high hematocrit, using a modifier on the claim form. If the provider has not reduced the dose or informed CMS that a dose reduction has occurred, however, Medicare's payment systems will apply a 25 percent reduction in payment. The provider is given appropriate notice of the payment reduction and may appeal the determination.

Promoting Ptient Savety through Hematocrit Monitoring

Consistent with the approach taken to advance all of its quality and transparency initiatives, CMS worked closely with the ESRD community and other stakeholders in developing the revised hematocrit monitoring policy. CMS announced its intent to develop the new policy in fall 2003, along with a solicitation of scientific literature from the industry. In the interest of promoting quality and efficiency in the care of ESRD patients, CMS was determined to develop a permanent, evidence-based policy for erythropoietin payment and hematocrit monitoring.

Scientific literature submitted to CMS demonstrated that patients with hematocrit levels within the target range had better health outcomes than those with hematocrits below the target level. The data also demonstrated that there is considerable natural variability in individual patient hematocrit levels, making it difficult to consistently maintain a hematocrit within the narrow range of 33–36 percent.

After analyzing the literature CMS developed a proposed policy, published in July 2004. The CMS reviewed available scientific evidence along with a large volume of public comments from the stakeholder community in developing the final policy. The final policy issued in November 2005 reflected a careful balance to ensure proper patient care while allowing appropriate payment for services rendered by treating physicians. In attempting to implement this policy, CMS became aware that there were process issues in collecting the claims-based information necessary to adjudicate these claims and, after working with stakeholders and CMS contractors, a revised erythropoietin monitoring policy was issued in April, 2006.

Appropriate interpretation of the evidence for erythropoietin treatment of anemia in the ESRD population is disputed within the stakeholder community. Several reasons for this dispute are not readily amenable to correction by CMS. In addition, many clinical trials have methodological restrictions that limit the degree to which their findings can be generalized among the Medicare population. Other published reports of clinical trials do not necessarily present all of the available data due to

[2] The FDA labeling for Epogen® and Aranesp® notes that as the hematocrit approaches a reading of 36, the dose of the drug should be reduced by 25 percent.

limitations of space and other factors. It is possible that some of the outstanding questions could be addressed in part by analyzing collected but unpublished data.

CMS believes that, in general, medical decisions are best made by the treating physician. The human physiologic response to erythropoietin is not immediate, and the effect of a given dosage on the hematocrit or hemoglobin of a given individual can vary widely. This variation also is reflected in the wide and unpredictable variation in the dosage needed to achieve and maintain hematocrit within the target range, although other factors also contribute to variation in dosage. Current accepted medical practice may also include the use of drugs for indications that are not covered by an FDA label, but that are supported by clinical evidence in peer reviewed medical literature. Medicare may provide coverage for off-label uses of drugs and biologics when those items are considered reasonable and necessary.

Mainstream press has recently focused on two trials published in the *New England Journal of Medicine* (NEJM) regarding erythropoietin use in chronic kidney disease (CKD) patients. However, the study populations for these trials do not necessarily reflect the Medicare ESRD patient population. Both studies addressthe optimal target level for hemoglobin in CKD patients who do not yet need dialysis. It is possible, if not probable, that many of the study subjects were not Medicare beneficiaries because they were too young to qualify for Medicare and were not disabled. Only patients with ESRD, who require dialysis or transplant, are eligible for Medicare regardless of age or disability; other patients with CKD are not Medicare beneficiaries (unless their age or a disability qualifies them). This distinction is important.

Anemia management for patients with ESRD cannot be assumed to be the same for patients, often younger, with CKD (who do not yet require dialysis). The NEJM study authors did not generalize their findings to the ESRD population. Patients receiving dialysis are exposed to clinical situations that patients with CKD not requiring dialysis are not exposed to, including: artificial kidney membrane exposure; large fluid shifts during dialysis; anti-coagulation received while on dialysis; different medications or other treatments. Finally, ***the NEJM studies looked at patients who were intentionally maintained at high hematocrit levels (the clinical study, research goal), as opposed to the typical ESRD patient who may fluctuate periodically above a hematocrit of 39 percent, but is not maintained at that level (the clinical practice situation).***

In spite of the *NEJM* studies' focus on patients with CKD, not ESRD, CMS considers the findings significant. Any scientific study published in a peer-reviewed journal such as the *NEJM* will be subject to international scrutiny and examination. Experts review the study design, methodology, results and conclusions. CMS will be participating in that scrutiny, which may include the need to design and implement further randomized clinical trials.

CMS is committed to establishing and maintaining policies in all areas of the Medicare program that protect beneficiaries, promote efficient and appropriate use of medical interventions, and enable providers to render excellent care. In the case of ESRD, and specifically the monitoring policy for anti-anemia therapies, CMS is exploring a number of approaches to collecting additional data. The current policy was developed after carefully analyzing and weighing a significant body of data and clinical evidence from a variety of sources; additionally, the policy was reviewed and reassessed 6 months after its initial publication. CMS is just now beginning to obtain sufficient claims data to attempt to assess whether the monitoring policy is achieving its stated goals: encouraging providers to try to maintain hematocrits in the range consistent with FDA labeling and national clinical guidelines, while not paying for unjustified dosages that maintain patients outside that range. Additional data sources will allow CMS to continue this pattern of vigilant, ongoing assessment of the monitoring policy. Further data also could support the possibility of an alternative CMS policy for anemia management and treatment.

The current monitoring policy relies on data submitted on the claims form. This effort could be expanded; in fact, CMS already is pursuing a number of enhancements. Currently, claims data do not provide either the route of administration for erythropoietin or the size of individual doses. CMS is implementing changes that will introduce a 100 unit code to capture dosing information with greater precision and, in conjunction with line item billing, will permit tracking of individually prescribed doses versus an aggregate monthly total for facilities.

In addition, CMS is implementing requirements to include the route of administration on claims for erythropoietin administered to ESRD beneficiaries (not chronic kidney disease patients). Existing CMS survey data suggest that subcutaneous administration is employed in only 7 percent of hemodialysis patients, differs by geographic location (more likely in the Midwest and West), and differs by dialysis facility ownership. Inasmuch as studies have suggested that subcutaneous may be a pre-

ferred route of administration, potentially requiring lower levels of erythropoietin to achieve the desired therapeutic effect, data of this nature is critical to continuous evaluation of the hematocrit monitoring policy.

Using the information currently collected, CMS also is able to quantify monthly utilization of erythropoietin, though the accuracy of these data is limited to what providers report on the claims—typically including quantities of the drug that have been opened but not necessarily provided to any patient (referred to as wastage). These and other limitations result in current claims data providing only a limited picture of erythropoietin utilization and anemia management. Additional data would be helpful.

One possible approach is to collect data—such as the dosage of erythropoietin actually administered or additional hemoglobin / hematocrit measurements—through clinical trials. Such an approach is a challenge to implement, however. The CMS' authority to condition Medicare coverage on participation in clinical trials and collection of data is could be constrained by the Health Insurance Portability and Accountability Act, the Privacy Act, and other concerns.

Another approach might be to create registries of data submitted by hospitals and other facilities. Such registries could be a robust data collection mechanism, pursuing elements beyond what can be collected on the claim form. Before such an approach could be adopted, however, CMS must assess potential restrictions to requiring hospitals and facilities to report information to a registry. Provider burden also would be an important consideration.

CMS could consider requiring additional Clinical Performance Measures through the existing Quality Initiative. The CPM project collects clinical information on dialysis patients in order to measure and track quality of care received by patients in dialysis facilities. However, CPMs currently are collected on just a 5-percent sample of dialysis patients nationwide. It will take a number of years before CPMs can be collected more broadly—ideally for all dialysis patients—due to limitations in facilities' and with CMS' own data collection systems.

Bundled Payment

In addition to significant quality efforts, CMS is committed to efficient and appropriate payment for all Medicare providers. In the context of ESRD care, many have urged a shift from the current model of paying independently for dialysis treatments and separately billable drugs, to a system of bundled payment. CMS is generally supportive of such reforms, and has devoted resources to research and development of a system that encourages high quality and efficient care through mechanisms such as value-based purchasing.

The CMS believes that a bundled payment system should promote efficiency and clinical flexibility for ESRD facilities. The system should guard against incentives to under-treat patients or to "cherry-pick" patients in order to maximize facility profits. Accomplishing these goals will require (1) research to support the development of an adequate case mix adjustment for a fully bundled system, and (2) mechanisms to ensure beneficiary protections and promote quality care.

The CMS has made significant accomplishments towards implementing a basic case mix adjusted composite rate system, as required by the Medicare Modernization Act of 2003 (MMA). Following the MMA's enactment, CMS funded research activities to develop new case-mix adjustments, which were implemented in April 2005. Since then, CMS has pursued several research approaches that could be used in a demonstration of a bundled PPS for ESRD facilities.

At this point, CMS is continuing its research on approaches that achieve our goals related to quality and payment accuracy. Development of a payment model that addresses the substantial variation in the dosage of erythropoietin has been a key area of this research. We continue to devote a considerable amount of time and resources to developing an appropriate ESRD payment system, including further research on targeted case-mix adjusters and quality incentives. We expect to detail the results of this work in the report to Congress required by section 623 of the MMA and move forward with a demonstration to further test these approaches, as the law requires. We expect these efforts, coupled with prior research, will provide a well-informed basis for comprehensive ESRD payment reform in the future.

Conclusion

This Administration has made significant strides in promoting and ensuring quality care for ESRD patients. From the CMS Quality Roadmap and efforts under the ESRD Quality Initiative like Fistula First, to selecting a Chronic Kidney Disease—focused site under the Care Management for High Cost Beneficiaries Demonstration, to ongoing research in support of comprehensive ESRD payment reform, CMS is helping to improve quality and efficiency in the care of ESRD patients. The sig-

nificant strides made over the last 5 years have laid important groundwork for further improvement. The CMS will continue to build on these efforts, and looks forward to further work with the Congress and the ESRD community to achieve our common goals.

Ms. NORWALK. Before we start, if I might ask my colleague, the Chief Medical Officer of CMS, who is a nephrologist, Barry Straube, to sit with me, that would be great.

Chairman THOMAS. Welcome, Dr. Straube.

You indicated—and all of us, obviously, have been interested in this focus at the continuing increase percentage, now to 39; and your argument, as I heard it, was that this was done in an attempt to provide a payment regulation structure. Because, obviously, a physician should be the one to determine that level.

I guess the difficulty I have in responding to that is that, notwithstanding the FDA label position, the manufacturer itself responding to concerns about that, the studies that we now have, which certainly any scientific method needs to be duplicated, followed up, examined, CMS continues to increase the percentage; and the argument for it, as I hear from you, is that it is a payment construction.

Of course, we understand your need to create systems that assist you in making payments. In fact, the whole discussion of bundling is to try to change the payment system. I guess, based upon the studies that we have seen, which certainly have to be validated and duplicated, this is something that probably should not be looked at as a payment question, absent pretty clear evidence of what is happening on overdosage, which if you had kept the policy at, say, the FDA label which it was at one time of 33 percent we would not be having those consequences.

So, it is difficult for me to listen to a justification for a level driven by a payment policy, when all of the evidence I have heard is focusing on the medical. I understand you are not supposed to make the medical decision. But if that is the case, why would you then go ahead and change the FDA labeling? For payment purposes?

Ms. NORWALK. I think there are a couple of different points I would make, Mr. Chairman.

The first is that the change in monitoring policy over this past year was critically important because our prior policy was not doing an effective job in reducing the dosage of Epo. At 37.5 and a 3-month rolling average, it was phenomenally difficult for our carriers to implement and actually go after those providers who were actually overdosing on Epo. It was difficult for the providers to follow that rolling average.

So, we felt it important, in order to keep the dosage down, to readjust our policies so that carriers could follow as well as the providers; and I can—I will talk in a second about how exactly that policy works.

But I would like to point out a couple of things in the FDA label, because I think it is important for this discussion as we focus on the clinical need. Of course, understanding that this is something

that we have asked providers to follow, there are a number of things.

One, the label talks about the idea that sufficient time should be allowed to determine a patient's responsiveness to a dosage of Epo before adjusting the dose. In fact, the label talks about an interval of 2 to 6 weeks that may occur between the time of dose adjustment and a significant change in hematocrit levels. That is important because our payment systems are on a monthly basis.

Since it may take 2 to 6 weeks—in fact, at the longer weeks, 6 weeks—for that to adjust, we did not want to have a payment system that penalized a provider who was actually doing the right thing, because the patient, for whatever reason, has his own physiological change to the drug which had not yet gone into effect.

Moreover, the label talks about dose adjustment as saying that if the hematocrit level exceeds 40 percent, the dose of Epo should be withheld until the hematocrit falls to 36 percent. So, one thing that the label does do in terms of a number is not actually 39, which is our level for payment changes, but is in fact 40 before the dose would be withheld.

Chairman THOMAS. I understand that. That gets back, I guess, to an earlier question that still perplexes a number of us.

In dealing with the payment concerns in allowing for an adequate leeway for the medical decisions, was there any discussion at all about trying to go public and push the idea that perhaps no update for this particular area of Medicare services, as opposed to skilled nursing, as opposed to any of the others, would be one of the fundamental changes that you could make and that income from drug usage which is used to try to augment the fact that there is no update could easily be changed, which would be payment questions—instead of dealing with the dosage on payment questions, which continues the perverse aspect of a monopoly drug being overused to help compensate for the cost structure in what you are monitoring says is important for payment purposes?

Ms. NORWALK. I think——

Chairman THOMAS. In other words, you created a trough—not you, CMS—and CMS is staying in this trough in trying to control the payment structure. When all you had to do is take a step back and say they are not getting an update. They should be updated regularly like everyone else, and it should not be a monopoly drug.

For example, I would be interested in asking a question along this line, and that is that what we did with the part B drugs in MMA was to require a single rate based on sales across all settings. So my question then, going to this issue, would be: Why does Medicare and the beneficiaries pay more for Epogen Alpha per 1,000 units to treat anemia in a dialysis center, compared to the same 1,000 units administered to cancer patients in the physician office setting?

Clearly, part of Dr. Singh's and other testimony is that there is a whole lot more of an analogous relationship than it appears to be and that that goes to the payment question again on a monopoly structure. Why are you paying two different rates for similar usages?

Ms. NORWALK. One of the things that the MMA does under section 303(c) is require that single-source drugs be paid by ASP plus 6. That is in the physician office setting.

The interesting piece here is that when we looked at the OIG study—and I think the GAO has a table of this in its report—that if you look at the OIG study, the OIG study details what the acquisition costs were for Epo in 2005. The ASP plus 6 percent is slightly lower, depending on the quarter, relative to the acquisition cost.

For CMS to update—actually, we found this actually going down. So, in terms of whether there was an update, I am not sure that an update was necessary, that ASP plus 6 has actually come in slightly lower than the OIG's.

Chairman THOMAS. First of all, that is an arbitrary structure in dealing with a noncompetitive drug, for which I thought was inadequate at the time we wrote the bill. That is okay. My question is simply why, in two different settings, for similar uses, identical drugs are paid at different prices?

Ms. NORWALK. Well, they are both paid at ASP plus 6 percent. In terms of why is really an issue between the companies and their marketing side.

Chairman THOMAS. One arena is a competitive one and the other is not. Would that be one of the reasons?

Ms. NORWALK. It may well be that ASP plus 6 in the non-ESRD market is competitive and may reduce the rate. But at the end of the day for this, to solve this problem, I agree with the GAO and, clearly, members of this Committee who think that a bundled payment, including everything, including currently separately payable drugs, makes the most sense, provided that we can get it right to provide the quality for beneficiaries and appropriately risk adjusted.

Chairman THOMAS. Appreciate that position.

I do believe that I do want to communicate, notwithstanding the fact that you are new on the job, to those who have been dealing with this decisionmaking and who have been less than timely in responding to letters that Congress has written that you have had since 2003. You are moving forward on it. I believe the Congress will move if you do not. I am urging that you do.

Does the gentlewoman from Connecticut have any questions.

Ms. JOHNSON OF CONNECTICUT. Let me just inquire a little bit more about the demonstration project that you are working on and the apparent difficulty of establishing an appropriate case mix adjuster. Could you talk about that a little bit?

Then, also, could you talk about the issues raised by the preceding panel that implied that if you titrate up you can get to stability—I do not want to paraphrase them too flippantly, but it sounded like easily and reliably. If that is the case, does Medicare reimbursement policy encourage titrating up and does Medicare reimbursement policy take any position in regard to what is apparently a more cost-effective delivery system that is widely used of injection?

Ms. NORWALK. To your first question, Mrs. Johnson, in terms of the demo, one of the things that we have been struggling with internally with our report to Congress in putting this together, we have had an expanded bundle demo where we are working with

members of a FACA Committee that represents patient groups, clinicians and other stakeholders.

But we have struggled with the ability to predict resource utilization, which in a sense gets to some of the other questions that you are asking. Since that is the basis of a prospective payment system, we have taken longer than we would like to take. But given that 93 percent of this population is covered by Medicare, it is so critical that we get it right. For that reason and because so many of these patients are disproportionately either African American, Hispanic or American Indian, this is critical to be accurate, to get it as close to right as possible before it is implemented.

It is also important because of the small size of some of the facilities. There are a couple of very big chains here, but not all of them are big. Consequently, we want to ensure that we do not put the small companies out of business with our payment policies.

I think that the FACA Committee will be meeting again early next year; and, hopefully, we will be moving forward. As we get the research back, we will be working on our demonstration project at the same time we are writing our report to Congress as to not waste any time with either of those so we can get them done as quickly as possible to you.

In terms of titration—and one of the things I will ask, if it is okay, my colleague, Dr. Straube, to speak on the more clinical issues. But in terms of titration, generally one of things that the label talks about is the variability among patients. In the label it talks about one of the largest clinical trials, that approximately 65 percent of the patients required doses of 100 units or less to maintain their hematocrit levels at approximately 35 percent, almost 10 percent of patients required a dose of 25 units or less, and approximately 10 percent required a dose of more than 200 units to maintain their hematocrit at this level. So, there is a pretty significant amount of variability there.

You also asked about subcutaneous administration or—something that I was talking about in my opening statement—about the use of fistulas, and the fistula first policy. Very, very important. We would like to see more patients have access to this. We have been promoting that policy.

I would anticipate under a bundled payment system that we would see more use of this use of fistulas rather than being as a apart of the whole dialysis treatment. It may be better for patients, and I would anticipate that it would also reduce the amount of Epo that needs to be administered. So, that is why we have been supporting it.

Finally, if I may, Mrs. Johnson, I think that—I do not know if we have got copies of this, but one of things when we are talking about the payment policy here that we in no way at CMS would like patients to stay at a hematocrit level of 39. That is not our policy. But what happens is these patients may be at 39—the hematocrit level may be at 39 for between 2 and 6 weeks; and then they come down to a more reasonable range where we like to see it because of dosing changes, for example.

Over time—this is something in the American Journal of Kidney Disease—nearly 30 percent of patients in the first quarter of the year 2000 were at a hematocrit level that was over 12. But by the

end of the year only 5 percent from that initial group. So, the numbers actually decreased very significantly. So, that, over time, the number of patients who were persistently above 12 in hemoglobin levels had come down significantly.

You simply have a great deal of variability from one quarter to the next. That is something that we thought was important that our policy take into account.

Ms. JOHNSON OF CONNECTICUT. That issue of variability that you have just described, does that—in other words, if you are aiming for—if your policy is 33 to 36 percent, any bundled—any policy has to take into account that you can go above that and below that and not we lower quality treatment. Am I understanding you correctly?

Ms. NORWALK. That is exactly the point that we were concerned about.

One of the things that initially this Committee brought to CMS's or then HCFA's attention in the late nineties was in fact underdosing and that we have a policy that does not promote underdosing because we cut off payment too soon.

Likewise, I appreciate that there is a concern about overdosing, both for clinical reasons and I want to be sure that we are walking that very narrow line so that physicians can follow the label and do what is best for the patients and not be adversely impacted, that the patient not be adversely impacted by our payment requirements, something that is reasonable and necessary versus what might be safe and efficacious as the FDA determines.

Dr. STRAUBE. Mrs. Johnson, I think—just to reiterate a few of the points that Leslie made, and you have asked some important questions here. I think when I look back historically—and I have taken care of many patients with eopetin myself as a nephrologist—the first focus back in the late nineties was the fact that 42 percent of patients had a hemoglobin of 11 grams per deciliter or greater. So, there was a preponderance of patients who were very low, and research studies at that time clearly showed an association with increased morbidity and increased mortality for people under a hemoglobin of 11.

So, the trend of everybody involved with this, including Congress, recommended CMS at the time increase its hematocrit; and the 90-day rolling average monitoring policy that was put into effect then was to get people—and has gone from 42 percent to 82 percent in 2005 now——

Ms. JOHNSON OF CONNECTICUT. Eighty-two percent complying?

Dr. STRAUBE [continuing]. that are over 11 grams per deciliter.

The slide that Leslie has distributed to the Committee is very, very important. Because people who are correctly reporting that—at any given point in time there may be 30 or more percent of people who exceed the 12 grams per deciliter of the FDA label.

If you look at those patients who consistently stay above that label, as opposed to occasionally going above it, it does come down to only 5 percent.

Ms. JOHNSON OF CONNECTICUT. In other words, you do not want your payment policy to penalize some variation but just to penalize staying at high levels?

Dr. STRAUBE. Correct. Those patients who consistently exceed that level. Because most patients do have some variability; some patients considerable variability. It is in contrast to perhaps some of the comments in the first panel. I believe it is very difficult to maintain patients particularly in that narrow range of 33 to 36 percent hematocrit or 11 to 12 grams per deciliter hemoglobin.

Ms. JOHNSON OF CONNECTICUT. So, you are saying it is very difficult to maintain them. Because I tried to bring that out. How easy is stability? They basically all said it is easy.

Dr. STRAUBE. I think it is more easy in the chronic kidney disease patients who have less factors going on compared to dialysis patients. But that narrower range, 11 to 12, is difficult; and some patients just naturally will go in and out without actually doing anything.

When you are changing doses of erythropoietin, when you are being exposed to an artificial kidney membrane in a dialysis machine, when they have other illnesses going on with chronic inflammation and acute inflammation affecting the possible dose of Epogen, it is not easy.

Ms. JOHNSON OF CONNECTICUT. So, different categories of patients may need to be looked at slightly differently, or at least your payment system wants to be able to take into account case mix?

Dr. STRAUBE. Yes, indeed.

Ms. JOHNSON OF CONNECTICUT. Thank you. Thank you for these charts.

Mr. STARK. Thank you, Mr. Chairman.

Welcome to the Committee, Ms. Norwalk.

Ms. NORWALK. Thank you.

Mr. STARK. I just wanted to know, is there any—I do not know what a valid clinical study would be, but is there a valid clinical study—I will use that word—that provides clinical justification for not reducing the dosage until it gets to 39?

Ms. NORWALK. I think our point——

Mr. STARK. Is there any study that would support that that you know of?

Ms. NORWALK. To not reducing it?

Dr. STRAUBE. Mr. Stark, I do not believe for a general population there probably is such a study. I would agree. I think for individual patients there might be indications for not reducing it.

Mr. STARK. But you do not know of a clinical study?

Dr. STRAUBE. Not in terms of a general population, no.

Mr. STARK. Ms. Norwalk, it is my understanding that CMS created something called the Epo Monitoring Policy Group, right?

Ms. NORWALK. Yes.

Mr. STARK. They were supposed to advise CMS on policies dealing with Epo, right? Now what troubles me is that of the 24 members—I am looking at the list here of maybe 22—18 of them disclosed financial associations with Amgen or Johnson & Johnson. Would not that, in fact, indicate that there might be some prejudice on the part of the people that you picked to advise you on this policy?

Ms. NORWALK. Either that or they happen to know a fair amount about the topic. At the end of the day——

Mr. STARK. I know they did. But let's talk about DaVita, Incorporated and AAMA and Gambro Health Care. They are also putting a lot of our taxpayers' money in their pockets. When you got two-thirds of your supposedly independent advisors—if I may use term loosely—on the take from the people that we are paying $2 billion a year to, does not that raise the issue that maybe you are not getting the straight skinny?

Ms. NORWALK. I think it is important—and one of the reasons you have seen our monitoring policy, that it be put out publicly, it is important to get comment from across the board.

Mr. STARK. Oh, come on.

Ms. NORWALK. Whether it is that group or whether there is another group, and at the end of the day——

Mr. STARK. You and I are not doctors, but you are a very good lawyer. You would tear these guys apart on the witness stand in 2 seconds, if you found out how much money they were getting from Amgen. Look, you got the American Kidney Fund. Amgen funds their clinical fellowship program.

You have got DaVita—that is self-explanatory; the Kidney Care Partners, a lobbying group for all of the dialysis guys; the National Kidney Foundation; 19—almost $20 million in corporate donations from the platinum friends, Amgen, DaVita.

Ms. NORWALK. It is clear that you—how you feel about how much we pay them.

Mr. STARK. It is a cozy club, isn't it?

Ms. NORWALK. That is one of the reasons why it is so important that our Chief Medical Officer is a nephrologist. Barry is not allowed to be paid by any of these groups.

Mr. STARK. I understand. But he is getting advice from these guys. It just seems to me that the time has come to understand, you know, these guys are not Bechtel in Iraq, and we should be getting reasonable and decent advice.

It just seems to me that it is difficult to support, when you empanel this group, knowing that most of them, your organization—I am sure you had nothing to do with selecting them, but it does lead us to become somewhat suspicious that we are not——

Now I might say there is probably no nephrologist in the United States—I will give Dr. Singh a chance to get out of this—that has not received something from Amgen, a golf ball or a dinner or something over time. So, it might be very hard——

Ms. NORWALK. Absolutely.

Mr. STARK [continuing]. to find. Billy Bud would have been a good three-act play if he had not jumped in the first act. But, nonetheless, this does seem rather suspect, overloaded with lobbyists and people who stand to benefit financially, tremendously, just to be selected.

Chairman THOMAS. I do understand the normal reaction would be dollars paid to entities as a link that might occur.

I think you also have to take into consideration the fact that you are dealing with a monopoly drug; and, notwithstanding it is a monopoly, the Government, unwilling to create a surrogate monitor for those prices and the fact that their business is focused solely on use of that drug and the ability to put pressure on the availability, the cost or the linkage of that drug, may have as much to

do with the positions that people take than the dollar amounts paid——

That is just the other side of the coin, on allowing a monopoly not only in the private sector but in terms of those in Government positions making decisions.

I thank you for yielding.

Mr. STARK. I hope we will have a chance to explore this further in the months ahead; and we will have ask Chairman Thomas if he will agree, on a pro bono basis, to continue advising us for all of the work that he has done on this. Maybe we can come to a conclusion which would have us, I think, and what I think my principal concern is is that CMS is the only group here that we have heard from today—and this is the troubling part—that has not erred on the side of caution.

I do not buy—and you are the only one who suggests the lower limits are a danger. Dr. Singh says it is much less of a danger than going over. So, that I would hope that that could be the principal change in policy as we try and revise these payment standards.

Ms. NORWALK. Well, I would be interested in hearing Dr. Straube talk a little bit about the underdosing of this, which clearly was a problem once upon a time, as you wrote to us about it. It may well be that the literature has changed since then, but in terms of the side of caution I think that we are cautious.

We do require that providers use the FDA label as a policy. We tell our contractors that they can, in fact, perform medical review at lower levels than 39. I think we are working with what is reasonable and necessary with a patient population that even the FDA label admits to having variability and want to ensure that those patients who for whatever reason in a particular month or 6-week period may find their hematocrit level above 39 and the doctor does the right thing in reducing the Epo dosage, not wanting to penalize that doctor.

On the flip side of that, it is not reasonable and necessary to have a patient persistently at that hematocrit level of 39; and, consequently, that is why we are taking the payment reductions there. I just want to be clear that our policy is: Follow the FDA label.

Now I appreciate we may have—this CHOIR study is a new study. It is something that we would like to take into account, like to look at the data there. In particular, I would be interested in reviewing the data around the 11.3 population, because they, too, are going to have a bell curve, where they will have people on the bell curve that are above a certain number—above 12, I would suspect—and perhaps maybe at any point in time a number of patients that may be above 13 or 39, and not wanting to penalize even in that study—when the target was the appropriate target, not wanting to penalize physicians because a patient physiology was such that for a particular moment in time, a static moment, that patient was above 39.

Mr. STARK. Thank you.

Dr. STRAUBE. Mr. Stark, I think we do very seriously take Dr. Singh's study, for instance, and are considering that.

As you know, when a scientific study is presented in the peer review literature, it has to get first by the review board of the journal of which it is published. But, subsequently, the medical community

has to look at that article and put it into context, having scrutiny of the whole methodology behind it, as well as the conclusions.

We are going to be participating with that. I have already talked with Dr. Singh. We would like some more of his data. But we should also have caution against jumping to one—to taking action that might have perverse consequences if we jump too soon.

The bell curve—there is evidence that the bell curve that we have described in terms of what dosage patients require, when you shift patients from the high end to the left, that is, to lower hemoglobins, you drive other patients down below 11. As we talked about earlier, it is just as dangerous, if not more so, to have low hemoglobin and hemocratics. So, we do not want to have unintended consequences from jumping to take action from a study that has just come out and has not had full scrutiny yet.

Just to end, there was a report in the last week, as an example, reiterating some reports that have come out over the years that, for instance, patients who were End-Stage Renal Disease patients and are obese do better than non-obese dialysis patients. If we were to respond to that and say, gee, we ought to recommend obesity in all of our dialysis patients because their outcomes are better, I think people would not think that was a smart thing to do.

So, I think that we have to have some caution, although we are very seriously looking at Dr. Singh's research.

Chairman THOMAS. Thank you.

Dr. Straube, your last statement was, as far as I am concerned, absolutely insulting, coming from a doctor, indicating an example of what you would not do, okay?

Number one, I think you need to seriously consider that your payment policy is killing people, okay?

The gentleman from California introduced a letter in the record from 1997 because there is a whisper campaign going on utilizing data from statements from that long ago to try to intimidate, which is a typical practice in this area.

I did not even bother to introduce my letter from 1998, which is also being used. Because, frankly, there was a problem then. It was too low. At some point somebody has got to consider that perhaps it is now too high, okay?

Ms. Norwalk, for you to say it may well be that literature has changed since that time, what do you think that whole first panel consisted of?

Ms. NORWALK. That is my point. The point I have is that both underdosing and overdosing is something that is important.

Chairman THOMAS. Absolutely. Now we are focusing on overdosing, whereas letters from 1997 or 1998 were focusing on underdosing. In between those two periods, we have turned a monopoly into a multi-billion dollar proposition.

I will tell you, as far as the Chair is concerned and other Members of the Committee who are not here—and I can assure you that it is shared broadly by the Committee, perhaps not as vocally as the Chairman would present it—it is absolutely unconscionable for CMS to allow a monopoly drug to be bundled with other drugs in an attempt to force usage; and that is what is going on.

Ms. NORWALK. Well, I look forward to our report to Congress coming to you and be able to come up with a bundled system where payment—where we do not have separate payment.

Chairman THOMAS. I am not talking about that. I am talking about current practice in which we pointed that out to CMS, and I haven't gotten an adequate response. Why would you allow anyone to take a monopoly product—monopoly by the decision of policy, not by the uniqueness in the industry—to be bundled with other drugs that are also necessary, to create an artificial demand for a product in which they control the absolute existence of the business? That is what is going on right now.

Ms. NORWALK. So, your point is, the payment rate should be the same in the ESRD facility as the ASP plus 6 is in other payments?

Chairman THOMAS. No. My only point was, why would you take a drug which is a monopoly and allow the industry, the person who produces it, to bundle it with other products they are using to influence how much they can use and when, based upon a pure pricing policy that we have created? That is what we are doing right now.

Ms. NORWALK. So, when you talk about the monopoly—are you referring to the Neulasta and the bundling? Is that what your concern is?

Chairman THOMAS. I am concerned with any monopoly drug accompanied with others that are not in which there could be a control of supply, utilizing the monopoly drug as the key.

Ms. NORWALK. I misunderstood your original question. I apologize.

Chairman THOMAS. I am not trying to not to get into very narrow, particular examples. I would have that same feeling about any monopoly drug being allowed to be combined with others in which you can control the market and the purchase of other drugs, and CMS has not addressed that. We have pointed it out, we have asked you to respond, and we haven't had an addressing on that.

Ms. NORWALK. I think it is something that we will clearly continue to review. It is something that I would imagine that the Antitrust Division at Justice and the FTC should be reviewing. I also imagine that it is something that—it may have other implications for fraud and abuse.

Chairman THOMAS. I do not think we have to go through the Justice Department when all you have to say is, if we have created a monopoly by virtue of our decisions, you do not get to do that. You do not need the Justice Department to make the decision. Perhaps your lawyer side is genuflecting in that directing. Your medical side, which you are now beginning to learn, ought not to go in that direction, but simply say, if we are creating an artificial monopoly for you, you ought not to be able to do those sorts of things, or it won't be a monopoly. In fact, I think it should have a surrogate price, anyway.

Ms. NORWALK. We will go ahead and take a look at that particular issue and ensure, as we always do, that whatever our policy is it does not have impacts to the patient that are in any way, shape or form a negative, and appreciating, of course, that we want to always want to watch the public fisc, as we are required to do.

Chairman THOMAS. Where we are now is we have a payment policy that perhaps is killing people; and we are using $2 billion, the highest price paid in a relatively narrow area for the use of the drug through the payment policy, that may in fact be doing that. That is exactly where we are today.

Ms. NORWALK. Well, I will not quibble with your last part of the statement. I will look at that.

I would disagree that, respectfully, Mr. Chairman, I do not believe our payment policy in any way, shape or form is out to kill people. In fact, what it is intended to do is ensure that the physician has the ability to monitor where the patient is so that the physician can appropriately titrate the dose for that patient, for that patient's best interest.

Chairman THOMAS. I put it in that phrase because I have learned over the years—and this is the only way you can do it—that somebody is actually going to pay attention to what I say if I put it in that extreme position.

But just as we were not doing a medical service to those patients when we were underdosing, the argument that somehow we do not want to take away the opportunity on the upper end, with the understanding, not just the doctor making a decision but a perverse payment system in which the providers of the services are not given any kind of an ongoing periodic update, and that they have gone for literally decades without a payment, and that the only way they make the margin of the income is on a drug which is an artificial monopoly imposed by Government itself.

When you begin building that kind of a structure, to argue that you are not going to examine the upper level because you want to leave it to the physicians is to ignore the entire dynamic and let me say also ignore the kind of business practices that have been carried out by these people in the shadows for a number of years.

One of the reasons I want to compliment the people who are now putting out the kinds of studies which you are going to look at and are going to find they are good is the fact that within a 3-month period we have turned completely around that shadowy area in which various pressures have been carried on for years in which they cannot now be done, because it is clearly public, and that if that kind of behavior continues it will be exposed more in the popular press.

But we now have a series of studies I expect you to look at. You are new. It was 8 months that you were not there, that you did not respond to the letters that we wrote. But I expect to see where you are on your bundling package.

As the gentleman from California indicated, it will be pro bono, but he means I am going to be able to participate. I do not believe in life after death, but I do not believe retirement is death, either.

We are going to continue to look at this area for two fundamental reasons: I am very much concerned about the health of these patients, and I am very much concerned about the enormous dollar amount that will produce the kind of behavior in both the manufacturers of this and the users of it if we do not create an opportunity for medically appropriate alternate patterns to live.

We have a monopoly on the structure, we have a monopoly on the drug, we have a monopoly on what they are required to do be-

cause of the payment system. We have got to free it up, even if we free it up with an artificial competition structure; and, in my opinion, we are a little overdue from the Medicare Modernization Act of 2003.

You may not be able to get your risk adjustment right. You can deal with something like the monopoly payment structure. You can deal with something like—and I really applaud you on the fistula first. As far as I am concerned, that ought to be an incentive in the payment structure to allow those various functions.

All of those can be put in place without waiting for a risk assessment structure. Those are pure payment policies devoid of any concern about the dosage structure and the rest. I do not know why those are not done already.

Ms. NORWALK. We will take a look at that.

Chairman THOMAS. I appreciate every time you said, "We will take a look at that." What we are trying to tell you is we directed you in MMA. Taking a look at it is not enough. We expect behavior on a relatively short timeframe or I might be able, in a pro bono way, to convince Congress that we perhaps begin to move from a legislative point of view. That would not be the desired choice, but it will be a choice if we do not begin to see in the ancillary areas, not the core, changes.

Ms. NORWALK. As I noted, we hope to have the report to Congress research to us where we will be building the demo and the actual report to Congress itself in short order; and I hope to have the report to the Committee by the summer.

Chairman THOMAS. Thank you very much.

With that, the Committee stands adjourned.

[Whereupon, at 12:45 p.m., the hearing was adjourned.]

[Questions submitted from Mr. Johnson of Texas and Mr. Weller to Ms. Norwalk, and their responses follow:]

Question from Mr. Johnson of Texas to Ms. Norwalk

Question: As someone who is vigilant over taxpayer dollars, I appreciate the GAO being here today, and the way CMS has taken steps to check the economic incentives for the utilization of drugs in the ESRD program. But while removing incentives that might encourage the over-utilization of drugs may benefit the taxpayer, it's also very important to focus on ways to improve the quality of care provided to beneficiaries.

I have here a list of clinical studies [attached below] that suggest that more frequent dialysis—which is often provided in one's own home—may significantly reduce the need for Epogen and other costly medications.

Earlier this year, MedPAC raised some issues with the payment surrounding home dialysis in its March report to Congress. Is CMS exploring other potential policy changes that support more frequent dialysis, which may reduce the clinical need for Epogen while improving the quality of life for the patient?

[The studies referred to by Mr. Johnson of Texas are being retained in the Committee files.]

Answer: Yes, the Centers for Medicare & Medicaid Services (CMS) is exploring other potential policy changes that support more frequent dialysis. Currently, there are two clinical trials in frequent dialysis sponsored by National Institutes of Diabetes and Digestive and Kidney Disease (NIDDK) and CMS. The goal of these trials is to test the clinical outcomes relative to daily hemodialysis (five or six times per week) compared to conventional hemodialysis (three times per week). The trials are expected to be completed in 2010 at the earliest. Data collection has already begun, starting in 2005.

Question from Mr. Weller to Ms. Norwalk

Question: The Hearing Notice cited that "Between 1998 and 2003, ESRD treatment spending increased by almost 50 percent." Obviously, we want and need to be good fiscal stewards of the Medicare Program. My concern is that we're jumping to conclusions on over-utilization of EPOGEN with no accounting for ESRD patient growth, how co-morbidities affect the treatment (for instance, diabetes is a major contributing factor to ESRD—does that affect spending), the increased frequencies of those co-morbidities, and the fact that the ASP system has driven down Medicare payments for drugs and biologics since 2003 (including for EPOGEN). Further, the EMP is now in place to catch any doctors who are dosing patients to maintain them above the target hemoglobin levels. Don't you think we need to move slowly and be fully informed prior to legislating on the ESRD program?

Answer: Yes, we agree that additional information on the appropriate use of erythropoietin stimulating agents (ESAs) in the treatment of anemia is needed to develop a more complete picture of its effect on different patient populations. Precipitous action could actually harm patients unless we are clear regarding the benefits to be gained from policy changes in this area.

The recent FDA black box warning for erythropoietin and darbepoietin clearly indicates that there is significant concern that Medicare beneficiaries may be harmed by these drugs. This warning was precipitated by a number of new clinical studies relevant to the use of ESAs to treat anemia in cancer patients. In light of this recent research and the FDA warning, we have taken immediate steps to address patient safety concerns for the non-ESRD Medicare population, such as opening a national coverage analysis on the use of ESAs for conditions other than ESRD. In addition, we made sure that Medicare's local claims processing contractors were aware of the FDA warning. We understand that, following the FDA warning and the subsequent revision of the compendium citation, most if not all local Medicare contractors have reviewed their policies on the use of ESAs in beneficiaries whose anemia is related to cancer

For Medicare beneficiaries with ESRD, we are working closely with the FDA to better understand potential patient safety concerns associated with the use of ESAs to treat this patient population. In May, the FDA will be holding an advisory Committee meeting to discuss the use of ESAs in cancer treatment. CMS is working with the FDA to plan a similar advisory Committee meeting on the use of ESAs for patients with chronic kidney disease and ESRD to be held later this year. In addition, we have been discussing safety concerns regarding the use of ESAs in ESRD patients with renal professional associations, large dialysis organizations, academic medical centers, pharmaceutical companies, and other interested parties to gather as much information as possible. In the course of gathering this information, it has become apparent that additional research is needed to address all of the questions being raised about the use of ESAs for this patient population. As a result, CMS has begun preliminary discussions with the National Institutes of Health about the possibility of collaborating on a large clinical trial of ESA effects in ESRD patients to assess these patient safety issues. At the same time, CMS is reviewing its recently improved ESA monitoring policy and is in the process of implementing a requirement for the use of modifiers to identify the route of administration of ESAs. All of these actions will help produce the information that is needed to support more definitive conclusions in this area.

Question: At the end of the day, aren't physicians responsible for hemoglobin levels and the EPO doses?

Answer: Yes. Medicare policy for the ESRD setting is intended to ensure that medical decisions are made by physicians, generally adhering to national guidelines and expert recommendations, such as the Kidney Dialysis Outcomes Quality Initiative (KDOQI) guidelines. However, our payment policy takes the FDA label safety issues into account.

Question: In a recent New England Journal of Medicine article there was reference to patients being treated with Procrit in the CHOIR study at an average hemoglobin level of 12.6 grams per deciliter. From the testimony today, it is clear that CHOIR was a clinical trial and that patients were

being treated toward a target hemoglobin that exceeds the FDA label for EPOGEN.

Another problem I'm having with details of this study is that these were non-dialysis patients that were treated as part of a clinical trial. Lastly, I understand that CHOIR study did not follow the gold standard of a double blinded design. Therefore, I don't see how findings from a clinical trial on non-dialysis patients can be linked across to ESRD patients. If Medicare dialysis patients were being maintained at this level, wouldn't these patients be flagged by the EMP and their doses reduced per the new CMS policy?

Answer: The new Medicare policy was not in effect during the CHOIR study. As mentioned earlier, the Medicare policy is intended to ensure that medical decisions are made by physicians and is consistent with the FDA label and current kidney disease industry guidelines to maintain a target hemoglobin level in the range of 10 g/dl to 12 g/dl.

[Submissions for the record follow:]

Statement of American Society of Pediatric Nephrology, Indianapolis, Indiana

The American Society of Pediatric Nephrology (ASPN) appreciates this opportunity to submit testimony for the record of the Committee on Ways and Means hearing on "Patient Safety and Quality Issues in End-Stage Renal Disease Treatment." The ASPN is a professional society composed of pediatric kidney specialists whose goal is to promote optimal care for children with kidney disease and to disseminate advances in the clinical practice and basic science of pediatric nephrology. The ASPN currently has over 600 members, making it the primary representative of the pediatric nephrology community in North America.

Background

Anemia is a complication of kidney disease, known as Chronic Kidney Disease (CKD) or kidney failure, and End Stage Renal Disease (ESRD) or Stage V CKD. Patients with kidney failure suffer from anemia because their kidneys do not produce a hormone (erythropoietin) that regulates red blood cell production. Anemia directly affects a pediatric patient's quality of life, including neurocognitive development, school attendance, exercise capacity and family support,[1] making proper anemia management critical to a patient's well-being. One of the key medications used to treat anemia in this population of patients is recombinant human erythropoietin (rHuEPO), commonly referred to as EPO.

Doctors determine a patient's degree of anemia with simple blood tests, measuring the hemoglobin level. The hemoglobin levels that define anemia in children with kidney disease differ from those in adults, as they depend on the age and gender of the patient. In the case of those patients who are then treated with EPO, the existing National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI™) or KDOQI™ opinion-based guidelines recommend a target hemoglobin level of 11.0 to 13.0 g/dl, for children up to 19 years of age. Treatment thresholds in anemia management should always be individualized to the needs of the patient, allowing a trained professional, in consultation with the patient, to determine the optimal dosing of EPO.

In light of the recent studies published in the *New England Journal of Medicine*, ASPN agrees that it is essential for the kidney care community to continue examining all available data to ensure that public policies reflect appropriate anemia management for all patients, both children and adults, with kidney disease and kidney failure. However, it is important to point out that no reliable scientific studies have been published that examine optimal hemoglobin levels for children with CKD. For this reason, the ASPN requests that Congress commission a study through the National Institutes of Health to test and evaluate optimal hemoglobin levels specific to children with kidney disease. Armed with this scientific literature, the kidney community and government can work to promote the safest practices with the highest quality of care for children with this chronic disease. ASPN is committed to working with clinical researchers to carry out such scientific studies.

Children Are More Vulnerable Than Adults

It has been said that children are not little adults, and this is especially pertinent in the treatment of children with both CKD and ESRD. Proper EPO dosing must

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[1] *American Journal of Kidney Diseases,* S90–S92 (May 2006).

take the age of the patient into consideration. Furthermore, and in contrast to the adult patient, the developing minds and bodies of children with kidney disease places them at a disproportionate risk in the event of inappropriate anemia management. Poor statural growth, impaired nutrition and abnormal cognitive development are all potential adverse outcomes of poor anemia management that mandate prospective study.

Children Have Unique Treatment Needs

Once children are diagnosed with CKD or ESRD, it is critical that the pediatric nephrologist be able to adequately target the proper hemoglobin level for the patient. Due to their size and age, a child's body will respond differently than adults in similar stages of CKD or ESRD. Consequently, pediatric treatment needs are unique in several ways:

- Children need different dosages of erythropoietin than adults—not only because they are smaller, but also because the way their bodies metabolize the drug may be different than what occurs in adults.
- Children sustain unique developmental and psychological responses to kidney disease and kidney failure. The identification and optimal management of these disorders in children and their relationship to anemia management requires professionals with expertise in pediatric nephrology.
- Most importantly, there are distinct differences in the frequency and type of coexisting illnesses that characterize the adult and pediatric CKD populations which may result in the optimal hemoglobin targets for children and adults receiving EPO to be different.

Conclusion

ASPN appreciates the opportunity to provide these comments to the Committee. The kidney community is largely unified in communicating a concern that actions taken by Congress and the Centers for Medicare and Medicaid Services (CMS) to revise anemia management guidelines must be based on all available scientific literature. The recent studies published in the *New England Journal of Medicine* only address the adult chronic kidney disease population. For this reason, it is imperative that further anemia management studies be conducted in all CKD and ESRD populations, including children, to ensure that revised government policies reflect sound scientific evidence.

The Society remains dedicated to providing the highest standard of care and ensuring patient safety for our nation's pediatric kidney disease patients.

Statement of Amgen

Mr. Chairman, Mr. Rangel and Members of the Committee,

Amgen is pleased to submit this testimony for the record of the Committee on Ways & Means Hearing on patient safety and quality of care for Medicare beneficiaries with End Stage Renal Disease (ESRD).

Amgen, one of the biotechnology industry's founders and pioneers, delivers vital medicines to fight serious illness. Amgen scientists have discovered and brought to market novel therapies that have helped millions of patients. Today, with a robust pipeline of potential new medicines, Amgen is investing billions of dollars in research and development to bring promising new therapeutics to patients.

I. The Benefits of EPOGEN® (epoetin alfa) for Treating Anemia in KIDNEY DISEASE

Chronic kidney disease is an increasingly recognized and important public health issue, affecting approximately 20 million Americans. The most advanced stage of chronic kidney disease is ESRD. Patients at this stage have inadequate kidney function to rid the body of harmful toxins, and it is fatal unless treated with dialysis, an artificial means of filtering the blood. In 1972, Congress enacted legislation ensuring that people with advanced kidney failure would be able to receive dialysis and other potentially life-saving treatments under Medicare.

ESRD patients are highly vulnerable, and there are more than 300,000 people with kidney failure being treated with dialysis in the United States today. Approximately one-third are African-American, and 1 in 5 are Hispanic. The mean age of dialysis patients in the U.S. is approximately 65. Dialysis patients typically carry a heavy burden of other medical conditions, including high blood pressure, diabetes, heart disease and anemia. Given these facts, it is not surprising that the survival

rate of dialysis patients is quite low. In fact, approximately 1 in 5 dialysis patients die every year—a death rate as high as that seen with many cancers. Indeed, patients who require dialysis are very sick, and the health care professionals who care for them are highly specialized in their understanding of how best to treat this precarious patient population.

Over 90% of ESRD patients develop anemia, a serious health condition that places patients at increased risk of hospitalization and mortality.

The kidneys produce a hormone called erythropoietin, which signals the body to make red blood cells in the bone marrow. Red blood cells carry life-sustaining oxygen from the lungs to all the vital tissues in the body. Without enough erythropoietin, patients develop anemia, or low numbers of red blood cells. Anemia is measured by a lab test called hemoglobin. Healthy people have hemoglobin levels in the 14–16 grams per deciliter (g/dL) range. If untreated, dialysis patients have hemoglobin levels that are much lower, often in the range of 8–10 g/dL or lower.

Anemia affects approximately 9 out of every 10 dialysis patients.[1] Patients with anemia suffer from severe fatigue and markedly reduced quality of life. Anemia increases the likelihood of being hospitalized and using more health care resources.[2,3] In addition, dialysis patients with anemia are at risk for cardiovascular events like heart attack or stroke. And dialysis patients with anemia are more likely to die than those without anemia.[4]

Before the advent of EPOGEN® more than a decade and a half ago, physicians had few options for treating anemia in ESRD patients, and had to rely on blood transfusions. Unfortunately, blood transfusions put patients at risk for complications such as blood-borne infections and iron overload. Blood transfusions also limit the chances for patients to successfully receive kidney transplants.[5]

EPOGEN® has reduced the need for blood transfusions and improved health-related quality of life in dialysis patients.

Amgen has pioneered the development of innovative medicines that safely and effectively treat anemia. EPOGEN® was developed by Amgen scientists using recombinant DNA technology, and has the same biological effects as naturally occurring erythropoietin. EPOGEN® was approved by the FDA in 1989 for the treatment of anemia in patients on dialysis.

The availability of EPOGEN® as a medicine to treat anemia has been one of the major breakthroughs in treatment for dialysis patients. Patients who are treated with EPOGEN® have a dramatic reduction in the need for red blood cell transfusions, and their quality of life is markedly improved by reducing fatigue symptoms, increasing energy level, improving physical function, and improving sleep.[6,7]

II. Quality of care and Safety profile of EPOGEN® in esrd

In its hearing notice, the Committee appears to have specific concerns about safety and quality of care with regard to anemia treatment in ESRD. Amgen shares the Committee's concerns for patient safety and quality of care and appreciates this opportunity to respond and to correct misinformation that the Committee has received.

EPOGEN® has enabled the safe and effective treatment of anemia in patients with ESRD.

EPOGEN® has been shown to be safe and effective in multiple clinical trials and has over a decade and a half of safety monitoring of real world use in more than 1.5 million dialysis patients. When used according to its FDA-approved label, EPOGEN®'s safety profile is well-established and widely known. The most frequently reported adverse events are detailed in the product's label, which accom-

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[1] USRDS 2006 Annual Data Report

[2] Collins AJ. Li S. Ebben J. Ma JZ. Manning W. Hematocrit levels and associated medicare expenditures. *American Journal of Kidney Diseases.* 2000 36(2):282–293.

[3] Collins AJ, Li S, St Peter W, Ebben J, Roberts T, Ma JZ, Manning W. Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. J Am Soc Nephrol. 2001 Nov;12(11):2465–73.

[4] Roberts TL, Foley RN, Weinhandl ED, Gilbertson DT, Collins AJ. Anaemia and mortality in haemodialysis patients: interaction of propensity score for predicted anaemia and actual haemoglobin levels. Nephrol Dial Transplant. 2006 Jun;21(6):1652–62.

[5] Lietz K, Lao M, Paczek L, Gorski A, Gaciong Z. The impact of pretransplant erythropoietin therapy on late outcomes of renal transplantation. Ann Transplant. 2003;8(2):17–24.

[6] Eschbach JW, Abdulhadi MH, Browne JK, Delano BG, Downing MR, Egrie JC, Evans RW, Friedman EA, Graber SE, Haley NR, et al. Recombinant human erythropoietin in anemic patients with end-stage renal disease. Results of a phase III multicenter clinical trial. Ann Intern Med. 1989 Dec 15;111(12):992–1000.

[7] Evans RW, Rader B, Manninen DL. The quality of life of hemodialysis recipients treated with recombinant human erythropoietin. Cooperative Multicenter EPO Clinical Trial Group. JAMA. 1990 Feb 9;263(6):825–30.

panies every vial of the product that is sold. Recent safety concerns have arisen from experiments which target and maintain hemoglobin levels above those recommended by the FDA (discussed in later section).

Quality of care for anemia treatment in dialysis patients is measured by the percentage of patients whose hemoglobin level is maintained > 11 g/dL.

While the FDA label directs clinicians to target a range of 10–12 g/dL, U.S. clinical practice guidelines reflect a review of the totality of evidence[8], including United States Renal Data System (USRDS) data showing that dialysis patients who have hemoglobin levels of 10–11 g/dL have an 18% increase in their risk of death and an 8% increase in their risk of being hospitalized when compared to patients with hemoglobin levels between 11–12 g/dL.[9] At the recent annual meeting of the American Society of Nephrology in San Diego last month, Allen Nissenson, M.D., Professor of Medicine at UCLA reminded the community that clinical practice guidelines state that ". . . Hemoglobin should be 11.0 g/dL or greater." He noted that this evidence-based recommendation was the result of review of 22 randomized, controlled clinical trials and evaluated a number of key clinical outcomes such as mortality, cardiovascular events, hospitalization and quality of life.[10]

It is well documented, in both domestic and international studies, that maintaining patients with a hemoglobin of less than 11 g/dL is associated with increased hospitalization, healthcare expenditure, and mortality.[11,12,13] This finding has been reflected in the National Kidney Foundation (NKF) 2000 and 2006 K/DOQIT Guidelines. Moreover, CMS has developed and implemented clinical performance measures (CPM), which can be used to assess the quality of care in dialysis facilities across the U.S. One CPM (or quality indicator) has been defined as the percentage of patients with a hemoglobin level greater than 11 g/dL. This same quality indicator has been employed in Europe through the European Best Practices Guidelines (EBPGs) and in Australia through Australian guidelines.[14,15]

In addition to the wealth of clinical data that supports maintaining hemoglobin levels above 11 g/dL, there is strong evidence that this is also cost-effective. Data from the USRDS demonstrate that patients who achieve hemoglobin levels between 11–12 g/dL save the Medicare system approximately $675 per member per month as compared with patients who achieve hemoglobin levels between 10–11 g/dL.[16]

Importantly, there have been tremendous improvements in the quality of care for dialysis patients over the past decade. According to the USRDS 2006 Annual Data Report and the CMS 2005 Annual Report for ESRD Clinical Performance Measures Project, the percentage of patients with hemoglobin < 11 g/dL has decreased from 84% in 1991 to 17% in 2004, a remarkable achievement by the nephrology community for patients. In the past, efforts to modify policy to control utilization of EPOGEN® at the upper values of the hemoglobin range have actually increased the number of patients with hemoglobins below 11 g/dL. As a result, extreme caution

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[8] KDOQI; National Kidney Foundation. Clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease in adults. Am J Kidney Dis. 2006 May;47(5 Suppl 3):S16–85.

[9] Roberts TL, Foley RN, Weinhandl ED, Gilbertson DT, Collins AJ. Anemia and mortality in haemodialysis patients: interaction of propensity score for predicted anemia and actual hemoglobin levels. Nephrol Dial Transplant. 2006 Jun;21(6):1652–62. KDOQI; National Kidney Foundation. Clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease in adults. Am J Kidney Dis. 2006 May;47(5 Suppl 3):S16–85.

[10] Slides presented by Allen Nissenson, MD. Professor, David Geffen School of Medicine at UCLA at the 36th Annual American Society of Nephrology Meeting. San Diego, CA. November 2006.

[11] Wolfe RA, Hulbert-Shearon TE, Ashby VB, Mahadevan S, Port FK. Improvements in dialysis patient mortality are associated with improvements in urea reduction ratio and hematocrit, 1999 to 2002. Am J Kidney Dis. 2005 Jan;45(1):127–35.

[12] Locatelli F, Pisoni RL, Combe C, Bommer J, Andreucci VE, Piera L, Greenwood R, Feldman HI, Port FK, Held PJ. Anemia in haemodialysis patients of five European countries: association with morbidity and mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS Nephrol Dial Transplant. 2004 Jan;19(1):121–32.

[13] Volkova N, Arab L. Evidence-based systematic literature review of hemoglobin/hematocrit and all-cause mortality in dialysis patients. Am J Kidney Dis. 2006 Jan;47(1):24–36.

[14] Locatelli F, Aljama P, Barany P, Canaud B, Carrera F, Eckardt KU, Horl WH, Macdougal IC, Macleod A, Wiecek A, Cameron S; European Best Practice Guidelines Working Group. Revised European best practice guidelines for the management of anaemia in patients with chronic renal failure. Nephrol Dial Transplant. 2004 May;19 Suppl 2:ii1–47.

[15] Roger S; Caring for Australians with Renal Impairment (CARI).The CARI guidelines. Haematological targets. Iron. Nephrology (Carlton). 2006 Apr;11 Suppl 1:S217–29.

[16] Collins AJ, Li S, St Peter W, Ebben J, Roberts T, Ma JZ, Manning W. Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. J Am Soc Nephrol. 2001 Nov;12(11):2465–73.

must be exercised when considering any policy changes that may affect this precarious population.

Hemoglobin levels fluctuate and must be measured repeatedly over time.

When targeting hemoglobin in the 10 to 12 g/dL range, hemoglobin values will fluctuate. Because of the constantly changing environment of a dialysis patient's body, the same individual will be more or less anemic and will sometimes react more strongly to EPOGEN® and sometimes less, thus having excursions above and below the target hemoglobin range. For example, infections are known to lower hemoglobin and erythropoietin responsiveness, while iron supplementation will help increase both. Thus, the physician must monitor hemoglobin and adjust the EPOGEN® dose as needed with the goal of keeping the patient's hemoglobin level in the target range for as much time as possible. These temporary hemoglobin fluctuations are universally understood by practicing nephrologists, and have been described in multiple publications using USRDS and other data.[17,18]

The USRDS data cited in the Committee hearing notice states that 40% of dialysis patients have hemoglobins over the FDA approved label of 12 g/dL. However, this USRDS estimate is at a single point, or "snapshot", in time, which does not give an accurate picture of anemia management.

Dr. Collins, who leads the analysis of USRDS data, describes the percentage of patients at a single point in time that have a hemoglobin level above 12 g/dL or above 13 g/dL. The recently reported figures appear to have raised concerns that physicians may be targeting higher hemoglobin levels than those recommended by the FDA or established guidelines. However, because of the routine and expected fluctuations in hemoglobin levels, it can be extremely misleading to draw any conclusions from a single hemoglobin measure without considering how physicians respond to the hemoglobin level.

Dr. Collins and colleagues state ". . . hemoglobin levels in almost 90% of patients seem to be in flux across the K/DOQI target boundaries such that a cross-sectional assessment of anemia management cannot give an accurate picture of anemia treatment."

In 2005, Dr. Collins published a paper demonstrating that in the vast majority of cases, providers responded promptly to temporary elevations in the hemoglobin level by appropriately adjusting the dose and bringing patients back into the target range.[19]

III. existing scientific evidence does not provide justification for congress to introduce new legislation

Several recent studies have raised concerns regarding the benefit-risk profile of EPOGEN®.

Recently published studies do not provide the definitive information needed to guide policy decisions.

The first paper, by Zhang and Cotter et al, is an article that analyzes medical claims data generated by Medicare in an attempt to link greater EPOGEN® use with higher hematocrit levels and increased mortality.[20] Zhang and Cotter conclude that high EPOGEN® doses are associated with an increased risk of death. This analysis suffers from a distortion commonly referred to as "confounding by indication" bias. Confounding occurs when another variable (the confounder) other than that being studied affects the outcome and leads to a false conclusion. For example: Analysis of Medicare data has shown that people who visit the doctor more often are significantly more likely to die. Therefore, it could be concluded that visiting doctors causes people to die! Of course, this is not the case. In reality, sicker patients see the doctor more frequently and sicker patients are more likely to die than those who are less ill. The same is true for Epoetin utilization. Sicker patients typically require more Epoetin to achieve the desired hemoglobin response, and sicker patents are also more likely to die.

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[17] Ebben JP, Gilbertson DT, Roberts TL, Foley RN, Collins AJ. Hemoglobin Level Variability: Associations with Comorbidity, Intercurrent Events, and Hospitalizations. Clin J Am Soc Nephrol 2006 1(6):1205–1210.

[18] Lacson E Jr, Ofsthun N, Lazarus JM. Effect of variability in anemia management on hemoglobin outcomes in ESRD. Am J Kidney Dis. 2003 Jan;41(1):111–24.

[19] Collins AJ, Brenner RM, Ofman JJ, Chi EM, Stuccio-White N, Krishnan M, Solid C, Ofsthun NJ, Lazarus JM. Epoetin alfa use in patients with ESRD: an analysis of recent US prescribing patterns and hemoglobin outcomes. Am J Kidney Dis. 2005 Sep;46(3):481–8.

[20] Zhang Y, Thamer M, Stefanik K, Kaufman J, Cotter DJ. Epoetin requirements predict mortality in hemodialysis patients. Am J Kidney Dis. 2004 Nov;44(5):866–76.

Mr. Cotter and colleagues acknowledge this important limitation in their paper (p. 874): *"this study has 2 noteworthy limitations. First and most important, when interpreting patient outcomes associated with prescribed epoetin dose, treatment-by-indication bias may exaggerate hazards and obscure benefits."*

A more recent analysis, presented at the American Society for Nephrology, replicated the Cotter analysis but introduced more comprehensive adjustments for 'confounding' using appropriate methods. This study found no association between mortality risk and EPOGEN® dose.[21]

The New England Journal of Medicine (NEJM) recently released the results of two studies, CHOIR (sponsored by Johnson and Johnson and CREATE (sponsored by Roche).[22,23] These studies examined the effects of more aggressive anemia treatment, not consistent with the FDA approved prescribing instructions, in kidney disease patients who were not receiving dialysis.

The CHOIR study treated anemic patients with chronic kidney disease with Procritr (Epoetin alfa), targeting a hemoglobin level of 13.5 g/dL versus a control group targeting a hemoglobin of 11.3 g/dl. In the CHOIR study, adverse events, including deaths, were greater in the group with the targeted hemoglobin of 13.5 g/dL.

Amgen takes the recent results of these trials very seriously. However, there are some limitations in the CHOIR study which make drawing definitive conclusions challenging. The gold standard in clinical research is the randomized, double-blind, placebo controlled trial, and this was an "open label" study where both clinicians and patients knew they were receiving Procritr, and the dose of the drug. Importantly, there was an unusually high drop-out rate in this trial (38% of patients), raising concerns about the ability to draw conclusions from the data presented. Most importantly, this study was not conducted in patients undergoing hemodialysis.

In a recently published article, the principle investigator for CHOIR, Dr Ajay Singh stated: "It is important to note that, unlike the Normal Hematocrit or the Canada-Europe studies, both CHOIR and CREATE evaluated pre-dialysis patients and so the results may not be generalizable to the dialysis community."[24]

Importantly, this was an experiment conducted to test practices that are not consistent with the FDA label or the way that Amgen promotes the use of EPOGEN®. The results of this study reaffirm Amgen's commitment to using the FDA-approved prescribing instructions to inform clinicians about how to use EPOGEN®. In U.S. clinical practice today, there is little evidence that clinicians purposefully maintain hemoglobin levels above the FDA-approved target range. Thus, the risks associated with persistently elevated hemoglobin levels seen in the CHOIR study and other experiments should not be applied to the transient elevations in hemoglobin levels described in dialysis patients treated under real world conditions.

Amgen promotes EPOGEN® according to the FDA label, and is proactively educating the clinical community about a recent FDA advisory for erythropoietic therapies.

In response to the CHOIR study, an FDA advisory was issued. Amgen is actively working with the FDA (in cooperation with Johnson and Johnson) to update the EPOGEN® product label with information about the CHOIR results and to inform prescribers. Amgen is proactively sending copies of the FDA advisory to all nephrologists, and our sales team is hand-carrying the advisory into physicians' offices. Amgen continues to recommend, as we always have, that physicians use our products in accordance with their FDA-approved labels. Although these studies in non-dialysis patients should not readily be generalized to patients receiving hemodialysis, we believe it is important for Amgen to help educate the clinical community about new scientific information, even if it is not definitive.

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[21] Wang et al. Exploring Relative Mortality and Epoetin Alfa (EPO) Dose Among Hemodialysis Patients. Poster presented at the 36th Annual American Society of Nephrology Meeting, San Diego CA November 2006.

[22] Drueke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, Burger HU, Scherhag A; CREATE Investigators. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006 Nov 16;355(20):2071–84.

[23] Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, Reddan D; CHOIR Investigators. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006 Nov 16;355(20):2085–98.

[24] Singh AK. The target hemoglobin in patients with chronic kidney disease. Nephrology News and Issues. 2006 Dec 20(13): p 29–30.

CMS coverage policy for EPOGEN®, as well as its claims monitoring policy for EPOGEN®, are consistent with the FDA approved prescribing instructions.

In the announcement for this hearing, concerns about patient safety and Medicare spending on anemia treatments in ESRD were raised. Further, the November 15, 2006 letter to CMS indicates a belief that current CMS policies for EPOGEN® establish "reimbursement incentives for providers to increase hemoglobin doses" and that these CMS policies are in conflict with FDA labeling.

Below, Amgen would like to address apparent confusion of the CMS *coverage* policy for EPOGEN® and a claims *monitoring* policy CMS employs to ensure it is paying for appropriate use. Since its inception, the CMS *coverage* policy for EPOGEN® has been consistent with the FDA approved label. The claims *monitoring* policy (also known as Erythropoietin Monitoring Policy or EMP) explicitly refers to the coverage policy for EPOGEN® as well as the FDA label in the manual instructions.

". . . While Medicare is not changing its coverage policy on erythropoietin use to maintain a target hematocrit level between 30% and 36%, we believe the variability in response to EPO warrants postponing requiring monitoring until the hematocrit reaches higher levels. For dates of services April 1, 2006 and later, CMS will not require contractors to initiate monitoring until the hematocrit level reaches 39.0 (or hemoglobin of 13.0). This does not preclude the contractors from performing medical review at lower levels. The Food and Drug Administration labeling for EPO notes that as the hematocrit approaches a reading of 36, the dose of the drug should be reduced by 25%. . . . Providers are reminded that CMS expects that as hematocrit approaches 36% (hemoglobin 12 g/dL), a dosage reduction occurs." Medicare Claims Processing Manual (CMS Pub. 100–04), ch. 8, ≤ 60.4

The CMS Erythropoietin Monitoring Policy (EMP) has evolved based on extensive scientific deliberation. The current policy represents an important improvement, focusing on* how *physicians manage anemia, by monitoring whether physicians appropriately adjust the EPOGEN® dose in response to elevated hemoglobin levels.

The EMP has evolved over time to account for the expected temporary fluctuations of hematocrit levels in different patients. When physicians target hematocrit levels of 30–36% (consistent with the FDA approved label hemoglobin target 10–12 g/dL[25]), the majority of those patients—even on a stable dose of EPOGEN®—will experience temporary elevations above 12 g/dL, as discussed earlier.

To account for these frequent temporary elevations, CMS has long recognized the need for a monitoring threshold above 36%. In 1997, CMS instituted monitoring for a 90-day rolling average hematocrit in excess of 36.5% (in effect, hemoglobins that were persistently above 12 g/dL). CMS revised this policy in 1998, implementing a 90-day rolling average where monitoring would occur when the hematocrit exceeded 37.5% (hemoglobin of 12.5 g/dL).

In April of 2006, after several years of extensive deliberation and consultation with clinical experts, CMS implemented a revised monitoring policy. Under the 2006 EMP, providers are still responsible for achieving the target hemoglobin in the FDA label range, and CMS expects that providers will follow the package insert and reduce the dose as hemoglobin levels approach 12 g/dL. If providers fail to reduce the dose of EPOGEN® when the hemoglobin exceeds 13 g/dL they are subject to a payment reduction.

Comments by former CMS administrator Dr. Mark McClellan, and by the CMS Chief Medical Officer Dr. Barry Straube, reiterate the importance of developing an appropriate monitoring policy that does not have a negative impact on the health outcomes of ESRD patients.

"Our Agency has worked to review the literature and consult with experts in the field to develop a means of monitoring erythropoietin usage without the risk of a negative impact on the healthcare outcomes of this vulnerable population. We are pleased to have found a reasonable means for monitoring erythropoietin dosages that are in line with the FDA-approved labeling for these drugs." CMS Administrator Mark McClellan, November 2005

"While we have to be concerned with patients who have hemoglobin [HGB] over 13 . . . Everybody has found that when you treat a group of patients, whatever the hemoglobin target is, if you lower that upper target range, you shift the hemoglobin levels. If the doctor tries to control everybody below 12, you will have other patients on the other end of the bell curve, below 11. And there are multiple studies, done

[25] Hematocrit is a percentage of packed red blood cells in a given volume of blood, and is approximately equal to 3X hemoglobin. Thus, a hematocrit of 36 corresponds to a hemoglobin of 12 g/dL.

in 1997 and 1998, that were associated with higher mortality rates, higher hospital admission rates and much higher complications—cardiovascular complications [when the levels dropped below 11]." CMS Chief Medical Officer Dr. Barry Straube, Inside CMS, November 28, 2006

Preliminary data indicate that under the new EMP, EPOGEN® doses and hemoglobin levels have slightly decreased.

Since the EMP went into effect April 1, 2006, Amgen analysis shows the average dose of EPOGEN® used in dialysis has decreased 2 percent. The average hematocrit has also decreased slightly in the few months since the new policy implementation, suggesting that the policy is having its intended effect of enforcing appropriate utilization. CMS's Dr. Barry Straube states that CMS claims data, as well as data from dialysis clinic Fresenius, demonstrate that hemoglobin levels have fallen since the implementation of the EMP. The impact of the EMP needs to be assessed over a longer period of time, but again, short-term analyses suggest that the policy is enforcing appropriate utilization.

IV. Medicare Expenditures for EPOGEN®

The Committee raised concerns about Medicare spending on EPOGEN® in the announcement for this hearing.

Increased Medicare spending on EPOGEN® reflects growth in the ESRD population, and substantial improvements in the quality of care.

Growth in Medicare spending on EPOGEN® results from several factors. One factor is growth in the ESRD patient population, approximately 3% per year. A major factor has been the tremendous increase in effective anemia management, reflected by improved achievement of the CMS clinical performance measure, reducing the percentage of patients with hemoglobin below 11 g/dL. As previously stated, this percentage has decreased from 84% in 1991 to only 17% in 2004.[26] Finally, the patient profile has changed over time. Today, more ESRD patients have other serious conditions which impact anemia and anemia treatment. For example, from 1995 to 2004 diabetes as the primary cause of renal failure has increased from 36% to 46%, and the number of patients with cancer has gone up 30%.1 As expected, this improvement in hemoglobin outcomes is correlated with increased EPOGEN® utilization.

Importantly, increasing Medicare expenditures on EPOGEN® are not the result of higher prices. In fact, CMS per unit expenditures for EPOGEN® have decreased 14% in recent years, from the statutory rate of $11 per 1,000 units that was in effect in the early 1990's to the current market-based ASP + 6% reimbursement of $9.446 per 1,000 units in Q4 2006.

The hearing announcement contained estimates of increased costs associated with the purported overuse of EPOGEN®. These estimates are incorrect and based on a flawed study and should not be used as the basis for policy-making. Policy based on the model in this study could seriously jeopardize the quality of care for ESRD patients.

The hearing announcement noted "a recent study from November 2006 in *Dialysis and Transplantation*[27] *that found that the population with a red blood cell count above industry guidelines also has higher drug costs, specifically, $3,100 per patient per year more just on the anemia drug.*"

The economic model (the Pizzi model) used in the cited study, while published, is seriously flawed. Specifically, the results depend on a flawed assumption that individuals should start and *remain* on 43,500 units of EPOGEN® a month without dose adjustments in response to hemoglobin levels. This assumption does not reflect K/DOQIT™ guidelines and is not consistent with the FDA approved prescribing instructions for EPOGEN® nor with published USRDS dosing patterns. Both the 2000 K/DOQIT™ guidelines and FDA label provide a starting range of EPOGEN® that doctors should use the first time a patient is given EPOGEN®, then instructs doctors to adjust the dose of EPOGEN® until hemoglobin is in the target range of 11–12 g/dL. In most cases, this results in a higher maintenance dose than the actual starting dose. The last time the average U.S. EPOGEN® dose approached the level assumed in the Pizzi model was 1992–1993. At that time, 84% of patients were below the recommended hemoglobin level of 11 g/dL.

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[26] USRDS 2006 Annual Data Report, CMS' 2005 Annual Report ESRD Clinical Performance Measures Project

[27] Pizzi LT, Patel NM, Maio VM, Goldfarb DS, Michael B, Fuhr JP, Goldfarb NI. Economic implications of non-adherence to treatment recommendations for hemodialysis patients with anemia. Dialysis and Transplantation. 2006 Nov; 35(11):654–732.

Adopting the dosing patterns portrayed in the Pizzi model could seriously jeopardize patient quality of care and significantly increase the percentage of patients with hemoglobin below 11 g/dL, increasing the risk of hospitalization and death and raising overall healthcare costs. The $3,100 per patient per year savings are not real, and unlikely to be realized given what is known about the current ESRD population. The *Dialysis and Transplantation* study should not form the basis of any policy decision, as it relies on faulty assumptions, makes projections based on off-label use of the product and is not consistent with the best available evidence.

When rigorously analyzed, the available data show that there is no systemic abuse of EPOGEN®.

In the November 15, 2006 letter to CMS, Chairman Thomas and Ranking Member Stark raised concerns about "systemic abuse" of EPOGEN®. Analysis of cross-sectional or "snapshot" in time analyses may give this appearance, but upon careful review of these and other data, EPOGEN® use appears appropriate and there is no evidence of systemic overuse.

Amgen has analyzed data from provider datasets that report hemoglobin values and EPOGEN® dosing on a per treatment basis, allowing for very granular analyses, even more granular than USRDS data that collect monthly information. A recent analysis of approximately 300,000 patients demonstrated that most physicians are using EPOGEN® in a manner that is safe and consistent with its FDA label. In fact, among patients who have ever recorded an elevation of the hemoglobin over 12 g/dL, over 50% of those excursions over 12 g/dL are managed back into the recommended target range within one month, and over 85% of those excursions within three months. These data support previous analyses19 which have demonstrated that patient hemoglobin levels are being appropriately managed when assessed over time using appropriate methods.

Moreover, the new EMP is fully aligned with the FDA label and will reinforce appropriate utilization of EPOGEN® by financially penalizing providers attempting to maintain patients at higher hemoglobin levels. The EMP notes that CMS expects that providers will follow the EPOGEN® label and reduce the dose as hemoglobin levels approach 12 g/dL and then requires an EPOGEN® dose reduction when a hemoglobin level exceeds 13 g/dL. If providers fail to reduce the dose of EPOGEN®, they are subject to a payment reduction.

Congress should not implement a payment system bundling dialysis services with separately billable injectable drugs (referred to as "bundled" payment) until the MMA mandated demonstration project is completed.

Amgen does not believe that Congress should consider moving to a single bundled payment for drugs and dialysis services in dialysis until the MMA mandated three-year CMS demonstration project is completed. The goal of the CMS project is to determine how best to include separately billable drugs in the dialysis composite payment.

A bundled payment system could be dangerous for patients, and end up costing the federal government more money. This is true for several reasons. First, unless bundling is accompanied by a robust scientifically valid risk adjustment system and an agreed-upon set of quality safeguards, it may result in perverse incentives to undertreat patients. Moreover, as evidenced by the broad and deep opposition of patient groups and medical providers, there are serious risks to rural patients and those in dialysis centers in underserved urban areas.

There are two critical elements necessary for the dialysis composite rate to be successful, and to assure that this vulnerable patient population is not harmed. The first is a robust and valid case-mix adjustment method—designing a system than can accurately predict which patients are most costly, and then adequately reimburse for those patients (a major goal of the CMS demonstration project). The second is a set of robust quality measures to safeguard patients against under treatment that may result from financial incentives that may limit their access to vitally necessary medical care. Congress recognized these requirements, and mandated the conduct of a demonstration project before implementing a bundled dialysis composite rate.

ESRD patients represent a seriously vulnerable patient group, at high risk of death. Even among ESRD patients, there are some who are more gravely ill and require significantly greater health care intervention. Unless Medicare appropriately reimburses for these patients, even one or two such patients in a single dialysis center can literally "tip the scales" and cause a dialysis center to lose money, and even risk closure. Many believe that the risk is highest for the small dialysis organizations that serve poor patients in rural areas.

Several models and real world examples have demonstrated this challenge and also the significant risk that a poorly designed system of bundled payment could have negative consequences for patient care.

- In 1989 Medicare paid for EPOGEN® at a rate of $40 for up to 10,000 units, a case rate. When CMS recognized that under this policy EPOGEN® doses were about half of what was needed, the policy was subsequently changed to pay per 1,000 units administered rather than at the case rate. This is an example of how fixed payments can result in undertreatment.
- A Medicare managed care capitation demonstration for ESRD resulted in higher costs than the fee for service comparison group. The additional costs to the federal government total approximately $18.5 million across the three years of the demonstration.[28]

An appropriate case-mix adjustment methodology has also been difficult to develop. A 1994 study by RAND and UCLA developed a method that was not shown to be adequate for dialysis patients.[29] A 2000 report released by the American Society of Nephrology and the Renal Physicians Association also attempted to create a case mix adjustment system, but was also found to lack the needed predictive power.[30]

"Capitation contracts put physicians at financial risk.accepting global capitation for a small group of patients may entail significant risk on the part of the capitated physician or health plan. It would be necessary to spread risk over many patients in order to reduce the financial risk faced by the physician or health plan to an acceptable level."

In summary, eliminating separate payment for dialysis drugs, if not implemented thoughtfully, could lead to unintended consequences including:

- Poorer quality of care, as dialysis units may need to make compromises to offset lower overall reimbursement.
- Higher overall Medicare costs as a result of poor quality dialysis care.
- Threats to access for poor and rural patients treated in small dialysis facilities. Small rural clinics may begin to avoid sicker/costlier patients in order to control costs, or close as a result of financial burden.

In conclusion, we want to thank the Committee for this opportunity to submit written testimony. We are proud of EPOGEN®'s long history of safely and effectively treating anemia in ESRD and stand with nurses, physicians, and other healthcare providers in supporting the best possible care for highly vulnerable kidney disease patients. Given the current state of evidence there does not appear to be justification for the introduction of new legislation. We remain concerned that legislation based on an insufficient analysis of scientific data could lead to negative outcomes for patients and for health care in the United States.

Statement of Richard Carrancejie, Birmingham, Alabama

Please, read the Birmingham news article on 11/18/06 on dialysis. we as patients are threatened everyday. the conditions are awful. we have roaches, untrained staff, the staff curse the elderly and black patients. our Medicare money doesn't go for or medical care. we are threatened by management and doctors with transfers or being taken off dialysis during treatment. most of the patients are afraid to speak out because they may be harmed. local officials do nothing because it involves a major employer [U.A.B.]. even the president of the college does not care. U.A.B. had to pay back millions last year to Medicare, they also lost the transplant records of 10,000patient.tyis is a nightmare. our state health dept. has not inspected since 1998. the positive room [blood disease] has been used by regular patients. the positive machines have been used all over the facility and on holidays. the Katrina victims have used our facilities, we do not know their fate, yet. it is a tragedy, a medical nightmare. we need help and protection from congress and the justice department. help us. this tragedy has gone on to long. individuals and company must be

[28] Summary report can be accessed at www.cms.hhs.gov/DemoProjectsEvalRpts/downloads/ESRD_Managed_Care_Summary.pdf

[29] Farley DO, Kallich JD, Carter GM, et al. Designing a capitation payment plan for Medicare end stage renal disease services. Santa Monica (CA), RAND. 1994.

[30] Bouchery EE, Gaylin DS, Rubin RJ, M.D., Shapiro JR, Held PJ. Lewin Group: Capitation Models for ESRD: Methodologies and Results. Prepared for Renal Physicians Association and the American Society of Nephrology. 2000.

punished and serve jail time for the death of so many patients. I have been on dialysis for three years, I have witnessed all these events. i have contacted the chairman of DaVita and the president of U.A.B., no reply. stop the Medicare money, have the FBI. and Medicare investigate, prosecute and make the companies and hospital repay the tax payers and put the worst law breakers away for along time.

Statement of DaVita Patient Citizens

Introduction

As America's largest dialysis patient organization, we are proud to represent over 20,000 pre-dialysis and dialysis patients and their families. On a wide variety of issues, we seek to ensure that the patients' point of view is heard and considered by policy makers so that continued progress may be made in the quality of care and life for patients with kidney disease. We appreciate this opportunity to submit testimony to the House Ways and Means Committee's Hearing on Patient Safety and Quality Issues in End Stage Renal Disease.

Quality of Life

Anemia is a serious, life-threatening problem affecting almost all dialysis patients. It causes fatigue, weakness and increased risk of hospitalization and death. In most cases, the administration of synthetic replacements for the hormone erythropoietin can manage our anemia and restore our energy. With appropriate anemia management, we require less medical attention and hospitalization, and we are better able to lead productive, quality lives.

The Experts on Quality of Care

Every dialysis patient's anemia situation is different. The decision of how to manage our anemia should therefore be made by our physicians in consultation with ourselves. Typical physician prescribing practices allow for physicians to use package inserts as a **guideline** for their prescriptions. Many of us enjoy higher quality lives because our doctors prescribe the appropriate amount of erythropoietin for each of us individually. This allows each of us to participate in the activities of daily living.

Research Applicable to ESRD Patients is Needed

Of course, it is critical that we, as well as our physicians, be informed of any increased risks associated with anemia management. The studies cited in recent news articles focused on Chronic Kidney Disease (CKD) patients in stages 1–4, who are not on dialysis. The studies did not focus on patients with End Stage Renal Disease (stage 5)—patients like us, who are on dialysis. We therefore look forward to clinical studies of anemia management in the ESRD population to determine the appropriate approach to anemia management for dialysis patients.

Community Cooperation Improves Quality of Care

Recognizing the importance of appropriate anemia management, we joined with the kidney care community in asking CMS to revise the April 2006 monitoring policy on anemia management to better align with physician prescribing methods and to take into consideration the patient's quality of life. We believe that this revised monitoring policy is a vast improvement over the April 2006 policy.

Conclusion

DaVita Patient Citizens greatly appreciates this opportunity to comment on ESRD patient safety and quality issues. We ask that, before proposing further changes to the CMS monitoring policy on anemia management, you take into consideration all of the data and the population to which it applies, as well as, the patients' perspective.

December 20, 2006

Dear Mr. Chairman and Members of the Committee,

The American Society of Nephrology (ASN) appreciates the opportunity to provide a written statement for the record regarding the issue of anemia management. We commend the Committee for its efforts to learn more about anemia management for individual's with kidney disease and kidney failure.

Through the Medicare program, the federal government has assumed primary responsibility for dialysis patients. The landmark 1972 (Medicare) legislation ensures that dialysis care is provided to this most vulnerable population. We continue to support innovative policy initiatives that reward improvements in care and the attainment of quality benchmarks based on scientific findings. Our Society and its members are dedicated to providing the highest standard of care and ensuring patient safety.

The ASN is a professional association with approximately 10,000 members. Of this membership, about 95% are physicians, with the remaining members basic scientists with a primary interest in renal disease. Virtually every licensed nephrologist in the United States is a member of the ASN, with an additional 3,000 nephrologists from 82 other countries comprising the remainder of our membership. The Society is focused on promulgating innovative research related to renal disease, and on providing continuing medical education to physicians and scientists dedicated to the improved understanding and treatment of renal disease.

In light of the recent studies published in the *New England Journal of Medicine,* ASN agrees that it is essential for the kidney care community to continue examining all available scientific data to ensure that public policies reflect appropriate anemia management for dialysis patients. We also reaffirm our ongoing commitment to work with the Congress and CMS to ensure that Medicare policy reflects the best science and ensures the welfare of patients, the public interest, and Medicare's stewardship of patients with kidney disease.

Anemia is a complication of kidney failure, also known as End-Stage Renal Disease (ESRD) and is a consequence of kidney disease in patients receiving dialysis. Patients with kidney failure suffer from anemia because their kidneys do not produce a hormone (erythropoietin) that regulates red blood cell production. Anemia has a profound physiological effect on every organ system (including the brain) and directly affects patients' quality of life. Anemic kidney disease patients have more difficulty performing every day activities, including maintaining employment. Physicians determine a patients' degree of anemia with simple blood tests, measuring the hemoglobin or hematocrit levels. A healthy man has a hemoglobin level of 15 (roughly a hematocrit level of45 percent), with slightly lower values in healthy women. Before effective treatment was available, a dialysis patient would typically have severe anemia with a hemoglobin level lower than 11 (hematocrit level of lower than 33 percent). Prior to the introduction of recombinant human erythropoietin (EPO) as a therapeutic agent in 1989, anemia management in dialysis patients was dependent on transfusions and other approaches which were largely ineffective.

ASN recognizes that the optimal target hemoglobin/hematocrit level for patients with kidney failure may not be straightforward. During the past 10 years, several observational studies have suggested that higher hemoglobin levels are associated with a lower risk of hospitalization and death, and higher levels of cognitive function.

However, recently two clinical trials published in the New England Journal of Medicine (NEJM) question whether higher hemoglobin targets are optimal for patients with kidney failure and have fostered a great deal of discussion within the scientific community. The CHOIR study indicated an association in kidney disease patients not yet on dialysis (patients diagnosed with Stages III and IV kidney disease) between higher hemoglobin levels and an increased risk for cardiovascular morbidity and death. The CREATE study (which was also published in the same November issue of the *New England Journal of Medicine),* in a similar group of patients with chronic kidney disease not on dialysis, found no significant difference in the combined incidence of severe adverse events between the higher and lower hemoglobin groups, although hypertensive episodes and headaches were more frequent in the former group.

A key component to any critical review of the scientific research data examining utilization of erythropoietin is patient variability in clinical response. Research has indicated that patient comorbidities, intercurrent events including hospitalization, and practice patterns contribute to this variability, which is not unique to patients with kidney disease. One recent study concluded that the variability in the response of hemoglobin levels to etythropoetin treatment over time in individual patients may account for moving 28 percent of all dialysis patients above and below the target hemoglobin levels during a one-year timeframe. Other studies support this finding as well. Because of this variability in patient physiology, optimal anemia management often requires a highly individualized approach to treatment.

ASN urges that Congress and CMS should take all available studies into account when setting Medicare policy. For example, the recent CMS EPO Monitoring Policy issued before the publication of the CHOIR and CREATE studies recognizes the need for reimbursement policy to take into account patient variability. When review-

ing this policy, it is important to understand that it is not a treatment guideline. Rather, it is an auditing tool. Under the policy, if a patients' hemoglobin reaches 13 and the dose is not reduced, then CMS will reduce the payment 25 percent. It does not call for, nor recommend, that patients' hemoglobin levels are maintained above 12 in accordance with the Food & Drug Administration label.

Congress should examine all of the available scientific literature before advising any policy changes. The recent trials should be reviewed along with those that are already a part of the literature, as well as the Food and Drug Administration package insert, to determine the optimal policies to be based on safety and efficacy. Policy should not be based upon the result of a single clinical trial. ASN is committed to working with the Congress and CMS to ensure that Medicare policy reflects the consensus of the scientific community.

ASN appreciates the opportunity to provide the Committee this statement for the record. ASN cannot emphasis enough that this debate on anemia management is about patient safety and quality of life, quality care and policy based and grounded in scientific findings. It is imperative that the scientific community and government work together to promote the highest quality of patient care. We look forward to working with the Committee as we continue to evaluate clinical data.

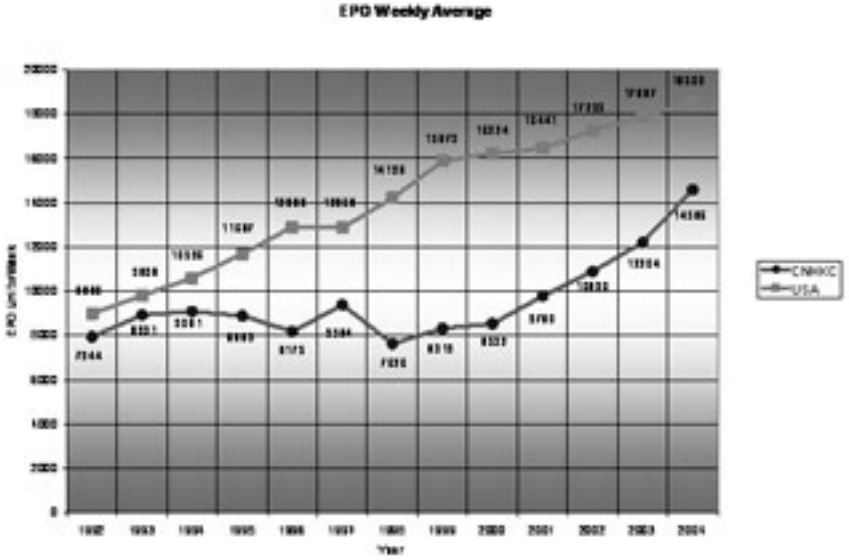
Sincerely,

, M.D.
President

Central New Hampshire Kidney Center
Laconia, New Hampshire 03246
December 19, 2006

Chairman and Members of the Committee on Ways and Means

I am a Nephrologist taking care of patients with End Stage Renal Disease for the last twenty years. I am the owner and medical director of Central New Hampshire Kidney Center (CNHKC) serving Laconia and the Lakes Region area of New Hampshire since 1990. As a physician, owner and administrator I had to make all the decisions that maintain my patient's safety, health and well being in addition to maintaining the financial viability of my dialysis unit. My choice was clear; patients and their needs always come first and have priority to any financial interest. Whenever a patient needed a medication he gets it because he needs it not because I will make few dollars off my patient. That was reflected in my use of EPO and how I was able to use 30—40% less drug than the national average. The following graph reflects the average weekly dose of EPO units used at CNHKC compared to the USA National average as reported by the USRDS.



In 1998 following the early results of the VA study"Subcutaneous Compared with Intravenous Epoetin in Patients Receiving Hemodialysis" which was then published by the New England Journal of Medicine, August 27, 1998 issue. http://content.nejm.org/cgi/content/abstract/339/9/578?ijkey=08d84b8e606283b32c14b90c4284b3eba947fa58&keytype2=tf_ipsecsha

I switched the method of administration of EPO from intravenous to subcutaneous and I noticed that my usage has dropped by more than 20%. Since then I continued to use this method of administration. Since 1998 I was using an average of 6000 units per week lower than the national average. This is equivalent to $3120.00 savings per patient per year for the Medicare and tax payers. By doing this I lost income that I could have generated from billing Medicare additional on average of $150,000.00 per year for the last 8 years. Also I lost rebates from Amgen because I did not achieve their required volume increase!!!!

As a physician and administrator I would like to share with you my experience and few important points that need to be addressed in this forum:

1. ***Method of administration of EPO:***

It is a puzzle for me that the subcutaneous method is not the standard method up till now. It is the standard method throughout Europe, Canada and the Veterans Administration. By the year 2002 about 70% of VA patients were switched to subcutaneous administration according to a VA press release http://www1.va.gov/resdev/news/press_releases/epoetin-022802.cfm

It is clear in the literature that approximately 20 to 30 percent of patients who receive EPO intravenously for the anemia of chronic renal failure may develop an elevation in diastolic pressure of 10 mmHg or more. In comparison, the blood pressure is less likely to rise after subcutaneous administration.

Also it is clear that the main advantage of subcutaneous EPO is its longer half-life: 24 hours versus four to nine hours when given intravenously.

So just by changing the method of administration this drug becomes ***safer*** and more ***effective*** and as an added bonus we will save the tax payers a lot of wasted money.

Why for all those years this is not the standard of care?? What's going on??

Why Amgen is not promoting a safer efficient way for using its drug??

Since August 27, 1998 an Amgen sponsored study was published in the New England Journal of Medicine "The Effects of Normal as Compared with Low Hematocrit Values in Patients with Cardiac Disease Who AreReceiving Hemodialysis and Epoetin" http://content.nejm.org/cgi/content/short/339/9/584, we learned from this study that higher hematocrit can kill dialysis patients. Yes, since 1998 not just in 2006 we learned that higher hematocrit can be dangerous to our patients. Did this prompt Amgen to ensure safety of its drug? On the contrary Amgen and its consult-

ants shoved the results of its own study under the rug and promoted achieving higher hematocrit!!

Why a chronic kidney disease patient receiving the EPO subcutaneously will get switched to intravenous once he starts on dialysis? Is this better for the patient or better for the bottom line? All of a sudden "it hurts"!! Yes, the bottom line!!

Those issues needs to be addressed and investigated as for the last eight years tax payers paid at least 20% more for an expensive drug and patients where unnecessarily subjected to potential worsening of their blood pressure, which is the major cause of morbidity and mortality in those patients, and probably was a contributing factor to the early death for some of those patients.

2. ***Rebates:***

This is a total disgrace to the practice of medicine. It is shameful to allow rebates for achieving larger volume for the use of a drug. It is shameful that the physician is forced to increase the dose of EPO for a patient who has hemoglobin of 10.8 or 10.9 so the center can meet the rebate threshold yet he knows that it will not do the patient any good. It is a disgrace that we submit patient's labs to a drug manufacturer so we can get a rebate.

This should ***STOP.*** It should have never been allowed. This is a shameful black spot on the practice of medicine.

3. ***Average Sale Price + 6%:***

What a joke? It will never cut on the use of drugs; it will make the fat cats fatter and it is not just killing patients it will also be killing the small providers and the competition or what ever left of it!! If the ASP of a drug is $1.00 this means that someone is paying $0.90 and another is paying $1.10 so the large provider will make a profit of about 18% and the small independent provider like me will lose about 5%. I don't think this is fair and it will never achieve what it is intended for. You have to level the field by using the Actual Sale Price or compensate the small provider different than the large provider. It is ridiculous that the small provider will end up contributing to the bottom line of Amgen and the large providers!!! That's why Fresenius made a deal with Amgen to be its sole provider of anemia drugs for the next five years to guarantee a lower price. This policy did nothing but gave Amgen the green light to keep increasing its price and Amgen delivered!!

4. ***EPO PRICE and COMPOSITE RATE:***

For each dialysis treatment I get paid an average of $130.00 while Amgen gets paid an average of $70.00 considering the current national average use per treatment. It is amazing that the price of this drug is more than 50% of the composite rate and yet the government is willing to pay??!!!. I have to provide 3–4 hours of nursing care, dietician, social worker, maintain equipment, maintain building and grounds, provide supplies, provide labs, insurance . . . etc. and yet on the other hand Amgen can decide it's own price no matter how ridiculous it is and increase it whenever it wants, no questions asked!!! The government controls the price for health care, the hospitals, clinics and physicians but when it comes to pharmaceuticals, they have a free ride. With the current drugs payment system as a small provider I end losing about 5% on EPO which means that I end up contributing to Amgen almost $3 every dialysis treatment. I don't think this is fair, this is nothing but ridiculous. It may be appropriate to let the free market work between the provider and the supplier but when the payer fixes the price on the providers that messes the whole picture, this economical concept is not an economy of capitalism not even economy of communism this is nothing but an **economy of terrorism** for the small provider. It is nothing but the pill of death for small providers. If the government wants to maintain healthy competition between providers then it will have to **fix the price** of EPO or force Amgen to sell it at a **declared fixed price** which is the same to every provider with no rebates or gimmicks. Amgen is a major partner in providing care for the ESRD program, Amgen had a free ride for many years and at this stage it needs to step up to its responsibilities and stop its practice of greed and back door gimmicks.

I hope by sharing my concerns and frustrations as a small provider you will have a better vision and understanding to what at stakes here as our main goal is providing the best care to our patients in the most efficient way and at the highest standards medically and ethically. I will be glad to answer any question.

Sincerely

Noshi Ishak, M.D.
CEO, Medical Director

Statement of Kidney Care Partners

The undersigned members of Kidney Care Partners (KCP) appreciate the opportunity to provide written testimony to the Committee regarding the intersection of anemia management and Medicare policy. We commend the Committee for its efforts to learn more about anemia management for individuals with kidney disease and kidney failure. Through the Medicare program, the federal government has assumed responsibility for the health and safety of dialysis patients. Therefore, it is appropriate that the Committee examine the optimum care patients should receive, including issues related to drug utilization.

KCP is a coalition of patient advocates, dialysis providers, physicians, nurses, and manufacturers. Our mission, individually and collectively, is to ensure: (1) chronic kidney disease patients receive safe and optimal care; (2) chronic kidney disease patients are able to live quality lives; (3) dialysis care is readily accessible to all those in need; and (4) research and development leads to enhanced therapies and innovative products.

Our members are dedicated to providing the highest standard of care and ensuring patient safety. The Centers for Medicare and Medicaid Services (CMS), the Government Accountability Office (GAO), the Medicare Payment Advisory Commission, and other organization have recognized the improvement of quality by the kidney care community during the last ten years. We continue to support innovative policy initiatives that reward improvements in care and the attainment of quality benchmarks. As part of our efforts, KCP launched the Kidney Care Quality Alliance, which has developed a starter set of quality-related measures that could be used to evaluate and reward high quality care in the kidney care community.

In light of the recent studies published in the *New England Journal of Medicine*, KCP agrees that it is essential for the kidney care community to continue examining all available data to ensure that public policies reflect appropriate anemia management for patients with kidney disease and kidney failure. We are committed to working with clinical researchers to determine the appropriate hemoglobin levels for these patients. We also reaffirm our ongoing commitment to work with the Congress and CMS to ensure that Medicare policy reflects the best science and ensures the welfare of patients, the public interest, and Medicare's stewardship of patients with kidney disease.

Anemia is a complication of kidney disease, which is known as Chronic Kidney Disease (CKD) and kidney failure, also known as End Stage Renal Disease (ESRD or Stage V kidney disease). Patients with kidney failure suffer from anemia because their kidneys do not produce a hormone (erythropoietin) that regulates red blood cell production. Anemia has a profound physiological effect [1] on every organ system (including the brain) and directly affects patients' quality of life.[2] Anemic kidney disease patients have more difficulty performing activities of daily living and maintaining employment. They experience lower vitality and may suffer from depression.[3] Doctors determine a patients' degree of anemia with simple blood tests, measuring the hemoglobin or hematocrit levels. A healthy man has a hemoglobin level of 15 (roughly a hematocrit level of 45 percent), with slightly lower values in healthy women. Before effective treatment was available, a dialysis patient would typically have severe anemia with a hemoglobin level lower than 11 (hematocrit level of lower than 33 percent).

There is a large and extensive peer-reviewed volume of literature discussing what the optimal target hemoglobin/hematocrit level for patients with kidney failure should be. For example during the past ten years, several observational studies have suggested that higher hemoglobin levels reduce the risk of hospitalization and death, while increasing cognitive function.[4] As one of these studies suggests, these

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[1] Morrell Michael Avram, et al., "Hemoglobin Predicts Long-Term Survival in Dialysis Patients: A 15-Year Single-Center Longitudinal Study and a Correlation Trend between Prealbumin and Hemoglobin" 87 Kidney Internat'l (Supp.) S6–S11, S9 (2003).

[2] Allen R. Nissenson & Lawrence T. Goodnough, "Anemia: Not Just an Innocent Bystander?" 163 Arch. Intern. Med. 1400 (June 23, 2003).

[3] Hans Furuland et. al., "A Randomized Controlled Trial of Haemoglobin Normalization with Epoetin Alfa in Pre-Dialysis Patients" 18 Nephrol. Dial. Transplant 353–61 (2003);

[4] S. Li & A.J. Collins, "Association of Hematocrit Value with Cardiovascular Morbidity and Mortality in Incident Hemodialysis Patients" 65 Kidney Int. 626–33 (2004); A.J. Collins, et al. "Death, Hospitalization, and Economic Associations among Incident Hemodialysis Patients with Hematocrit Levels of 36 to 39%" 12 J. Am. Soc. Nephrol. 2465–73 (2001); A.J. Collins, et al., "Hematocrit Levels and Associated Medicare Expenditures" 36 [282–93 (2000); F. Locatelli, et al., "Anemia in Haemodialysis Patients of Five European countries: Association with Morbidity and Mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS) 19 Nephrol. Dial.

Continued

outcomes could result in lower costs to the Medicare program. Specifically, it found that Medicare patients with hematocrit values of 36 to less than 39 cost the program significantly less than those patients with hematocrit values of less than 30.[5] Other prospective clinical trials have not observed benefits with higher hematocrit levels.[6] The FDA label recommends maintaining patients at a hemoglobin level of 10–12.

Two recent studies published in the *New England Journal of Medicine,* which have engendered substantial controversy and discussion,demonstrate the continuing debate within the scientific community. The CHOIR study[7] indicated an association in kidney disease patients not yet on dialysis (patients diagnosed with Stages III and IV kidney disease) between higher hemoglobin levels and an increased risk for cardiovascular morbidity and death. The CREATE study[8] (which was also published in the same November issue of the *New England Journal of Medicine*), in a similar group of patients not yet on dialysis, found no significant difference in the combined incidence of severe adverse events between the higher and lower hemoglobin groups, although hypertensive episodes and headaches were more frequent in the former group.

Clinical studies have found that determining optimal hemoglobin levels is also complicated by patient variability in their response to the drug. Researchers believe patient comorbidities, intercurrent events like hospitalization, and practice patterns contribute to this variability, which is not unique to the kidney care community. One recent study concluded that the variability in the response of hemoglobin levels to epoetin treatment over time in individual patients may account for moving 28 percent of all dialysis patients above and below the target hemoglobin levels during a one-year timeframe.[9] Other studies support this finding as well.[10] Because of this variability in patient physiology, optimal anemia management requires a highly individualized approach to treatment.[11]

Congress and CMS should take all available studies, as well as the Food and Drug Administration (FDA) label, into account when setting Medicare policy. For example, the recent CMS EPO Monitoring Policy, issued before the publication of the CHOIR and CREATE studies recognizes the need for reimbursement policy to take into account patient variability. When reviewing this policy, it is important to understand that it is not a treatment guideline. Rather, it is a reimbursement auditing tool. Under the policy, if a patients' hemoglobin reaches 13 and the dose is not reduced, then CMS will reduce the payment 25 percent. It does not call for, nor recommend, that patients' hemoglobin levels should be maintained above 12.

In addition to the EPO Monitoring Policy, Congress may also consider anemia management studies when discussing reforms to the ESRD payment system. If Congress is considering payment revisions that incorporate any or all separately billable drugs or biologics into the composite rate, it is vital that an appropriate case-mix adjuster be developed that accounts for the variability in patient response to medications and the lack of predictability. Currently, there are no universally accepted case-mix adjustors for patients on dialysis that address patient variability in drug utilization. In its attempts to develop an ESRD bundle, CMS has recognized the difficulties of accounting for this variability as well: "Implementation of a revised outpatient ESRD payment system without consideration of this patient specific varia-

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Transplant 121–32 (2004); N. Ofsthun et al., "The Effects of Higher Hemoglobin Levels on Mortality and Hospitalization in Hemodialysis Patients" 63 Kidney Int. 1908–14 (2003); E.G. Lowrie et al., "Medical Outcomes Study Short Form-36: A Consistent and Powerful Predictor of Morbidity and Mortality in Dialysis Patients" 41 Am. J. Kidney Dis. 610–9 (2003).

[5] Allan J. Collins et al. "Death, Hospitalization, and Economic Associations among Incident Hemodialysis Patients with Hematocrit Values of 36 to 39%" 12 J. Am. Soc. Nephrol. 2465–73 (2001).

[6] A. Besarab et. al., "The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin" 339 N Engl J Med. 584–90 (1998).

[7] Ajay K. Singh, et al., "Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease" 355 N Engl J Med 2085–98 (2006).

[8] Tilman B. Drueke, et al., "Normalization of Hemoglobin Level in Patients with Chronic Kidney Disease and Anemia" 355 N Engl J Med 2071–84 (2006).

[9] E Lacson et al., "Effect of Variability in Anemia Management on Hemoglobin Outcomes in ESRD" 41 Am J. Kidney Dis. 111–24 (2003).

[10] Norma J. Ofsthun, et al., "The Impact of the Change in CMS Billing Rules for Erythropoietin on Hemoglobin Outcomes in Dialysis Patients" To Be Presented at RRI International Dialysis Conference (January 2007).

[11] Norma Ofthun et al., "The Effects of Higher Hemoglobin Levels on Mortality and Hospitalization in Hemodialysis Patients" 63 Kidney Internat'l 1908–14, 1913 (2003).

bility may compromise patient access to quality of care." [12] In addition, it is critically important that if a bundle is adopted, Congress also provide an annual update mechanism that would allow CMS to provide updates to the base rate. Currently, the Medicare ESRD program is the only Medicare program without such an update mechanism. These challenges must be met before such revisions are made.

Congress should examine all of the literature before advising any policy changes. The recent trials should be reviewed along with those that are already a part of the literature, as well as the FDA package insert. Policy should not be based upon the result of a single clinical trial. KCP members are committed to continuing their work with experts in the kidney care community to determine appropriate hemoglobin levels for patients with kidney failure, as well as with the Congress and CMS to ensure that Medicare policy reflects the consensus of the scientific community.

KCP appreciates the opportunity to provide these comments to the Committee. Patient safety and quality care are at the heart of this discussion. It is imperative that the community and government promote the safest practices with the highest quality of care. We look forward to expanding upon our comments based upon today's discussion as well.

Abbott Laboratories
American Kidney Fund
American Nephrology Nurses' Association
American Regent, Inc.
American Renal Associates, Inc.
American Society of Nephrology
American Society of Pediatric Nephrology
Amgen
California Dialysis Council
Centers for Dialysis Care
DaVita, Inc.
DaVita Patient Citizens
Fresenius Medical Care North America
Genzyme
Medical Education Institute
Nabi Biopharmaceuticals
National Renal Administrators Association
Northwest Kidney Centers
Renal Advantage Inc.
Renal Physician's Association
Renal Support Network
Satellite Healthcare
U.S. Renal Care
Watson Pharma, Inc.

Statement of National Kidney Foundation, Inc., New York, New York

The National Kidney Foundation (NKF) is the nation's oldest and largest voluntary health organization serving the needs of patients with kidney disease (CKD) and the health care professionals who care for them. Our role is challenging since chronic kidney disease (CKD) patients often have multiple related diseases and complications including cardiovascular disease, hypertension, dyslipidemia, anemia, and bone and mineral metabolism problems. NKF appreciates the concern of the Ways and Means Committee for the quality of care for and safety of end stage renal disease patients. A similar dedication has driven the NKF's clinical practice guideline development program, known as the Kidney Disease Outcomes Quality Initiative (KDOQI).

Since its inception in 1995, NKF's KDOQI has transformed medical practice, community and public awareness, healthy policy, and patient outcomes. KDOQI's 12 evidence-based clinical practice guidelines have shaped the way we look at kidney disease and how it is treated in the United States and around the world. The KDOQI process has always relied on a structured review of the evidence and the independence of the work group assembled to review each topic. Updates to the original KDOQI clinical practice guidelines for hemodialysis, peritoneal dialysis, and

[12] Department of Health and Human Services, "Report to Congress: Toward a Bundled Outpatient Medicare ESRD Prospective Payment System" 22 (2003).

vascular access were published as a supplement to the July 2006 edition of the *American Journal of Kidney Diseases*. A new version of the KDOQI anemia guidelines, the *Clinical Practice Guidelines for Anemia of Chronic Kidney Disease,* was published as a supplement to the May 2006 issue of the *American Journal of Kidney Diseases.* The KDOQI anemia guidelines were originally published in 1997, and updated in 2001. This new guideline has been expanded to cover all stages of chronic kidney disease (CKD). Anemia often negatively affects the quality of life for patients with CKD. However, among all the potential complications of CKD, anemia is perhaps the most responsive to treatment.

The National Kidney Foundation has finalized plans for a formal review of new information that might have an impact on these recent recommendations from KDOQI on anemia management. This confirms KDOQI's announcement last month that it would continue its decade-long process of timely review of new data relevant to published KDOQI Clinical Practice Guidelines. The Co-Chairs of KDOQI have asked the anemia work group to reconvene on February 3, 2007, to discuss the implications of recently published studies and studies accepted for publication on anemia.

The first step in this process will be a structured review of the new evidence by the NKF Evidence Review Team headquartered at Tufts New England Medical Center in Boston. This evidence will then be examined by the work group to determine if it has a material impact on any recommendations made in the KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease published in May, 2006. When the anemia work group and the evidence center complete the analysis of the new studies for both safety and efficacy, appropriate announcements or publications will be developed.

This same concern for patient safety and quality of care for Medicare beneficiaries in the End Stage Renal Disease Program leads the NKF to urge Congress and the Centers for Medicare and Medicaid Services to analyze with caution the recommendations from the Government Accountability Office for bundled payment for dialysis services. We draw the Committee's attention to a Report that Secretary Thompson sent to Congress in 2003. The title of the Report is: "Toward a Bundled Outpatient Medicare ESRD Prospective Payment System." On page 22 there is the following statement: "Implementation of a revised outpatient ESRD payment system without consideration of this patient specific variability may compromise patient access to quality care." On page 31, "The changes in practice patterns resulting from a bundled ESRD (Prospective Payment System) will require monitoring to determine whether clinical outcomes improve or decline as a result of the system's financial incentives." On page 33, "Several of the K/DOQI clinical practice guidelines provide measures and minimum values of quality dialysis. Efforts to collect and evaluate such measures will be essential in order to ensure that clinical outcomes do not decline as facilities respond to the new financial incentives created by a bundled (Prospective Payment System)."

The recommendation for a bundled payment for dialysis services reflects a concern about the potential for over-utilization that exists under the current reimbursement policy. Nevertheless, a bundled system creates incentives for underutilization that could negatively affect dialysis patient outcomes. This is of particular concern in that higher doses of epoetin are required in the African American population, those individuals that have vasculitis as a cause of their kidney failure and cancers such as Multiple Myeloma (United States Renal Data System 2003 Annual Data Report). Also, patients with chronic infections and dialysis catheters also require more epoetin secondary to resistance to the medication. As far as anemia therapy is concerned, the effect of Medicare's early payment policy suggests that the threat of underutilization is real. Medicare initially provided a flat payment for erythropoietin, without regard to dosage. Under that payment system, dosage was low and there was little improvement in the anemia experienced by dialysis patients. There was also evidence of racial disparities that developed based on the responsiveness to treatment noted above (United States Renal Data System 2003 Annual Data Report). We are concerned that these areas need to be given careful consideration.

There are additional concerns about a bundled payment system that should be addressed. Many patients have bone and mineral metabolism disorders that require treatment with active vitamin D analogs. A bundled payment system could result in a substitution of oral vitamin D for injected vitamin D preparations. Not only would this shift cost from Medicare Part B to Medicare Part D, but the effect of vitamin D therapy could be much more dependent upon patient compliance. According to the United States Renal Data System 2006 Annual Data Report, only 65% of individuals with Employer Group Health Plan medication coverage routinely took their medications. This area should also be given careful consideration. The potential for undertreatment may also lead to elevated parathyroid hormone levels which

is associated with epoetin hyporesponsiveness, thereby compromising the bundled amount to cover this medication.

Similarly, we are concerned that a bundled payment system could lead providers to revert to the use of blood transfusions to treat anemia in dialysis patients who are not responsive to erythropoiesis stimulating agents. Not only would such a change in practice patterns expose this vulnerable patient population to unknown risks from the nation's blood supply but it would also make it difficult to consider these patients for kidney transplantation since the transfusions introduce antibodies that complicate organ matching.

These are only a few examples of the concerns with bundling. It was stated at the hearing that it would be possible to make retroactive adjustments should the bundling formula prove to be problematic. However, there will be no way to reverse the negative patient outcomes that could result from adoption of a bundled reimbursement policy that does not address these issues.

The National Kidney Foundation appreciates the opportunity to submit this testimony. The Committee members should consider the National Kidney Foundation as a resource while it continues to deliberate these issues. Thank you!

Statement of the Renal Physicians Association, Rockville, Maryland

The Renal Physicians Association (RPA) is the professional organization of nephrologists whose goals are to ensure optimal care under the highest standards of medical practice for patients with renal disease and related disorders. RPA acts as the national representative for physicians engaged in the study and management of patients with renal disease. RPA greatly appreciates the interest of Committee Chair William Thomas and Ranking Member Charles Rangel in the issues surrounding anemia management services provided to patients with kidney disease and kidney failure. We welcome the opportunity to offer our perspective on these complex issues. Our testimony will focus on the use of clinical practice guidelines and best evidence in healthcare delivery, the role of the nephrologist in the care of patients with kidney disease and the importance of maintaining physician prescribing autonomy, the issue of ESRD patient variability related to EPO dose, and common misperceptions regarding anemia management and reimbursement for these services.

Clinical Practice Guidelines and Physician Prescribing Autonomy

RPA believes that clinical practice guidelines in renal care, like those in other medical disciplines, should be evaluated on the basis of the strength of evidence, an assessment of harms and benefits, and should benefit from robust physician and other multidisciplinary input and review. Guidelines developed with these considerations in mind will enhance the delivery of high quality patient care and help ensure kidney patient safety. RPA also believes that the current body of literature in the area of anemia management fulfills these criteria, and forms a solid foundation for public policy making efforts such as the Centers for Medicare and Medicaid Services (CMS) recently finalized EPO Monitoring Policy (EMP). Further, it is our opinion that the CHOIR and CREATE studies recently published in the *New England Journal of Medicine,* once they have been subject to the full measure of robust scientific review, will likely represent an important addition to this already significant body of literature, and should be considered thoughtfully and thoroughly by care providers and policymakers.

However, RPA also feels compelled to note that clinical practice guidelines are in fact guidelines, not required protocols, and that the most important determining factor in the care of the patient should be the physician's clinical judgment considered in the context of the physician-patient relationship. RPA believes that it is of paramount importance to maintain the physician's autonomy and ability to exercise clinical judgment in prescribing for the individual patient. Decisions for the individual may and should be permitted to deviate from the norm on the basis of individualized clinical evaluation and specific patient needs. This is a fundamental and well-recognized clinical principle in medicine, and it is mandatory that it be maintained and protected. RPA believes the CMS' EPO Monitoring Policy accounts for such use of the physician's clinical judgment.

Variability in ESRD Patient Hemoglobin Levels

RPA believes that in the recent discourse on national coverage of EPO, the critical issue of variability of individual patient response to EPO dose has been understated. As noted in RPA's previous correspondence to CMS on EPO coverage policy develop-

ment, attempts to assess or quantify individual sensitivities (i.e. responsiveness) to EPO at a narrow level have not been successful. Thus,there is no single, predictable response to a given dose of EPO, a fact that accounts for the wide range in individual responses to treatment. As a result, in the aggregate it is physiologically not rational to tailor a normal distribution of patient responses to a payment limit: such a paradigm cannot be successful in delivering optimaltreatment with sophisticated agents to complicated patients. Payment limits structured in this fashion place emphasis on the wrong arm of therapy: emphasis should be placed rather on *reducing* the number of patients with low hematocrits/hemoglobins (>30%/10 gm/dL). At the same time, Medicare coverage policy should strive to maintain levels in all patients <11 gm/dL, given the ample data disclosing the adverse short and long-term effects to patients with persistent anemia. Simply put, overemphasis on monitoring patients at the upper end of the range should not create problems for patients at the lower end, and RPA believes that the current CMS EPO Monitoring Policy strives to avoid such problems in the broad Medicare ESRD beneficiary population.

Misperceptions Regarding EPO Requirement

Finally, RPA would also like to take this opportunity to dispel some common misperceptions regarding reimbursement for erythropoietin. There have been articles in both the mainstream and medical trade press implying that nephrologists have a financial incentive to prescribe higher doses of erythropoietin to ESRD patients. This is simply not true. Nephrologists prescribe EPO based on their clinical judgment of what will optimize the individual patient's hemoglobin level. Moreover, it is the dialysis facility that receives reimbursement for EPO prescribed to ESRD patients, not the nephrologist, and thus any inference that the nephrologist will personally benefit from prescribing higher doses of EPO, or any drug, to ESRD patients is erroneous.

Conclusion

In conclusion, RPA supports the use of clinical practice guidelines in the development of protocols enhancing the delivery of high quality patient care but believes they must be considered in the context of the physician's clinical judgment. RPA believes that physician prescribing autonomy must be maintained, and that the variability in ESRD patient hemoglobin levels must be accounted for in the development of national coverage policy for EPO. Finally, the misperception that nephrologists have a financial incentive to prescribe high doses of EPO to ESRD patients is erroneous. Once again, RPA appreciates the opportunity to provide our perspective on these issues to the Committee, and we make ourselves available as a resource to the Committee in its future efforts to ensure the best possible health outcomes and quality of life for Medicare beneficiaries with ESRD.

Statement of Kris Robinson, American Association of Kidney Patients, Tampa, Florida

The American Association of Kidney Patients (AAKP) (www.aakp.org), founded in 1969, is the nation's only kidney patient-led and managed education and advocacy organization for people with kidney disease. AAKP serves over one million Americans annually who have either lost kidney function (and live with dialysis or transplant) or have chronic kidney disease (CKD). As you may know, the *average* life expectancy for individuals following initiation of dialysis therapy is short, less than 5 years. As patients ourselves, we realize the important need to ensure quality of care and access for all dialysis and potential dialysis patients.

AAKP was instrumental in the fight for the enactment of the Medicare ESRD Program. In 1972, Shep Glazer, the Vice President of our forerunner organization, testified before the House Ways and Means Committee while being dialyzed. This effort was crowned with success in 1972 when Congress enacted the program that continues to provide Medicare funding for dialysis and kidney transplantation.

AAKP appreciates the opportunity to provide written testimony to the House Ways and Means Committee. We are available to assist the Committee with needed information as it continues to review quality of care issues for today's dialysis patients. AAKP's written testimony will provide patients' views on safety and efficacy in healthcare and provide insight into what patients need to ensure a high quality of life and health.

AAKP commends the Committee for assessing and reviewing patient safety and quality issues for care received by dialysis patients. AAKP's mission has always

been to help all kidney patients achieve the best possible quality of life and longevity.

Regarding specific issues under review by the Committee, AAKP has developed and distributed position papers on the following topics in recent years: 1). Support for the continuation of the patient and physician relationship in medical care; 2). Support for continuous quality care and improvement and 3). Support for continuous safety monitoring. The content of these positions is summarized below:

Patient/Physician Relationship—AAKP strongly believes the principle that a physician and patient must be permitted to decide a care plan best suited for that patient. Averages and other statistics are fine for certain purposes, but medicine is fundamentally about the treatment of a unique individual. In this light, we worry that any legislation that mandates particular treatment options may impede the doctor/patient decision-making relationship.

ESRD Continuous Quality Improvement—AAKP supports legislation to provide data on outcomes and quality of care for kidney patents. We worry that piecemeal approaches to improving quality may not offer the best health outcomes for patients and is why we have continuously asked Congress to establish a "National Commission on Improved Kidney Patient Outcomes."

Safety Monitoring—AAKP supports legislation to ensure safety in healthcare settings. We applaud Congress, the Centers for Medicare and Medicaid Services (CMS) and the renal community as a whole for developing programs to ensure safety for all patients. However, we wish to encourage Congress to look at the major safety issues that impact all patients.

With regard specifically to the administration of erythropoietin (EPO) to patients, AAKP has previously addressed CMS with comments and questions regarding dosing policies. Though recent clinical studies such as CHOIR have demonstrated mortality in non-dialysis patients, we have asked CMS "Is there any clinical data that demonstrates that dialysis patients—either nationally or regionally—are in fact receiving more EPO than necessary to maintain an appropriate hematocrit level, or that inappropriate EPO prescribing by physicians is the driver for increased EPO spending?" We are awaiting a response.

Furthermore, AAKP is also interested in how the issues currently being discussed about EPO will be affected by the "Medicare Prescription Drug, Improvement, and Modernization Act of 2003" (DIMA) (P.L. 108–173). In particular, section 623 of DIMA instructs CMS to implement effective January 1, 2005, a new "basic case-mix adjusted composite rate," which would, *inter alia*, transfer the dollar difference (the "spread") between acquisition and Medicare payment rates for separately billed drugs and biologicals (including erythropoietin) to the per-session composite rate for dialysis treatment. Even if there is some current law financial incentive for overutilization of EPO, would not that incentive be eliminated by section 623? We are concerned that section 623 has not occurred as scheduled.

National Commission on Improved Kidney Patient Outcomes—AAKP previously wrote to the House Ways and Means Committee calling for a "National Commission on Improved Kidney Patient Outcomes." We believe a global perspective—rather than a piecemeal approach—is needed to improve quality and coordination of medical care for dialysis patients, and perhaps even create savings to Medicare. Indeed, as payor for the medical care of about 75 percent of all kidney patients receiving dialysis in the United States, CMS bears a special responsibility to ensure that dialysis patients not only receive quality medical care—but that care is provided in a manner that maximizes positive outcomes. We would note the November 21 report by the HHS Inspector General calling for more collection of quality of care date in the ESRD program. AAKP believes these issues will become even more urgent as the nation's dialysis population is expected to grow three-fold over the next decade.

Moreover, in the kidney community today, there is a vigorous debate about the adequacy of medical care of dialysis patients, prompted by apparently higher U.S. dialysis patient disability, morbidity, and mortality in cross-national studies. Some have argued that it is a "national disgrace that the death rate now solidly stays in the region of 24% every year and has more than doubled over the last 30 years" (Kjellstrand, CM, Blagg, CR, "Differences in dialysis practice are the main reasons for the high mortality rate in the United States compared to Japan," *Hemodial Int*. 2003; 7(1): 70). Others believe that cross-national comparisons are flawed for selection reasons (i.e., sicker, older patients are denied dialysis in comparison countries) and that the U.S. should take pride in the unique availability of dialysis here (*see, e.g.,* Friedman, EA, "International comparisons of survival on dialysis: Are they reliable?" *Hemodial Int.* 2003; 7(1):59–66). In any case, with the U.S. ranking last among industrialized countries in mortality for kidney patients, there is a clear need to take a close look at the adequacy of medical care for U.S. dialysis patients.

Charged with a comprehensive program review, the agenda for such a National Commission might also include patient access to other important renal replacement treatments, such as home dialysis and transplantation; nephrologists' residency training; and reimbursement of rural facilities. There are also many other opportunities to improve care and reduce costs to Medicare, including slowing the progression to ESRD among chronic kidney disease patients (CKD), better chronic disease management, advances in new technology and biomedical solutions, more transplantation, and improved patient education. AAKP stands ready to assist the Committee on ways to implement such a Commission.

AAKP commends the Committee for addressing the issues of quality of care as currently delivered to the over 300,000 dialysis patients. We appreciate the opportunity to provide input into your efforts and look forward to working with you to provide continuous quality improvement to all patients.

Statement of Dori Schatell, Medical Education Institute, Madison, Wisconsin

The Medical Education Institute (MEI) is a non-profit foundation dedicated to the mission of helping people with chronic diseases learn to manage and improve their health. Since 1993, MEI efforts have focused on improving longevity and quality of life for people with chronic kidney disease (CKD) through health behavior research and evidence-based patient and professional education materials. I appreciate the opportunity to provide an additional viewpoint for the Committee.

To begin, I am dismayed by the implication that the K/DOQI Guidelines were influenced by industry participation. When the MEI administered the first DOQI Guidelines in 1996, I was the "writer" for the Anemia Work Group, recording their deliberations. Amgen requested and was denied permission to observe the proceedings of this Work Group—they read the final Guidelines at the same time as the rest of the renal community and had no role in the outcome. The clinicians who spent many months of intensive hours reviewing hundreds of scientific papers and developing recommendations were a dedicated, conscientious group who knew they were making history. I am very saddened to hear their labors and the subsequent results of groups that updated the National Kidney Foundation K/DOQI Guidelines denigrated and their ethics called into question. Industry support from Amgen and others for the original DOQI Guidelines and subsequent K/DOQI Guidelines has moved the practice of nephrology forward by helping to establish key clinical benchmarks in a number of vital areas of practice, including nutrition, bone disease, dialysis adequacy, vascular access, etc. Where would patients be today if those Guidelines had not been written? Who would have supported their development if industry had not stepped up to the plate?

Second, much of the criticism of current CMS policy regarding anemia treatment for people on dialysis is based on the recently-published CHOIR study. Having reviewed the results, which concluded that patients with stages 3–4 CKD had a 34% higher risk of adverse outcomes if their hemoglobin levels were 13.5 g/dL, several aspects of this paper were of sufficient concern to possibly call the conclusions into question:

- **Study power:** A power analysis revealed that 1,352 patients would need to be enrolled; data were reported for 1,432 patients on the basis of intent to treat. But 549 patients withdrew from the study without having had a composite event. Did this bias the findings?
- **Baseline differences between the high and low hemoglobin groups:** *There were significant differences in baseline data for cardiovascular history.* Those in the high Hgb group had a significantly higher rate of high blood pressure (p=0.03) and coronary artery bypass graft (p=0.05) prior to the study. Did this influence the results?
- **Differences in baseline GFR:** It is unclear whether the time to renal replacement therapy (RRT) analysis accounted for baseline variations in GFR. Clearly individuals with a GFR of 15 at baseline are much closer to needing RRT than those whose GFR was 50.
- **No blood pressure changes:** Despite worse cardiovascular outcomes in the high hemoglobin group, there were no significant changes in blood pressure in the high vs. low hemoglobin group. This seems odd.
- **Lack of statistical significance:** The CHOIR authors state that there were, ***"no significant differences*** *between the two groups in the four individual components of the primary composite end point* (hospitalization, MI, stroke, or

death). . . . *However, the hazard ratios for death and hospitalization for CHF had strong* ***trends*** *toward a higher risk in the high-hemoglobin group than in the low-hemoglobin group."* Also, the risk of heart attack (MI) with high hemoglobin was.91 (less than 1.00); thus those with higher hemoglobin actually had a *lower* risk of MI.

- **Non-standard measurement of quality of life:** It is unclear why three separate tools were used to assess quality of life (QOL). Given the *highly unusual* finding of no QOL benefit to a higher vs. a lower hemoglobin, one must wonder if patients were overwhelmed by the sheer number of survey items (a total of 83 questions, many with sub-questions). Multiple studies in CKD and dialysis patients have shown that those with higher hemoglobin levels score significantly higher in physical and mental functioning on the SF–36 and Kidney Disease Quality of Life (KDQOL).[1] [2] And, in the dialysis population, higher physical and mental functioning independently predict lower rates of hospitalization and death.[3] One of the tools used in the CHOIR study (LASA) was developed for breast cancer and has been used only twice before in kidney patients. Interestingly, in one of those two studies, 1,557 non-randomized predialysis CKD patients received r-HuEPO, and their hemoglobin levels rose from 9.1 g/dL to 11.6 g/dL in 16 weeks *with significant improvement in all QOL parameters.*[4] In the other analysis by some of the same researchers, there was *"a positive and significant relationship between Hb levels and QOL."*[5]

In light of these concerns—and of the exactly contradictory findings of the CREATE study in a similar population published in the same issue of the *New England Journal of Medicine*—the MEI urges the Committee to proceed with caution and consider all of the available data.

Third, previous CMS policies related to use of EPO to correct anemia in people on dialysis have had unintended consequences that have harmed patients. Early reimbursement of EPO offered incentives to undertreat patients when dialysis centers were paid $40 for up to 10,000 units and $30 additional for more than 10,000 units. The Hematocrit Measurement Audit (HMA) policy, which stopped EPO reimbursement to dialysis centers for patients whose hematocrit levels rose above a rolling average of 36.5%—without a provision to permit physicians to medically justify higher levels—led to lower average hematocrit levels and patients complained of a "roller coaster" effect that was very debilitating. Please see the attached article the MEI published in *Nephrology News and Issues* with patient interviews that illustrate in these individuals' own voices how difficult it is to care for children or grandchildren, do simple tasks around the home (like vacuuming, hammering nails, or washing windows), hold down a job—or even walk to the mailbox with inadequate anemia correction, and how very much better patients feel at a higher vs. a lower hematocrit. Anecdotally, patients report they feel every percent of difference in their hematocrit or hemoglobin. The MEI is concerned that bundling EPO with other drugs may, over time, lead to underutilization as dialysis centers attempt to hold down costs to compensate for inflation—*unless* an appropriate case mix adjuster is used *and* an annual update mechanism is created, as was proposed in the Kidney Care Quality and Improvement Act.

Fourth, each year, according to the United States Renal Data System (USRDS) half of the more than 100,000 individuals who reach end-stage and need dialysis or transplant to survive are *under age 65, or "working-age."* Enabling working-age patients to keep their job benefits:

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[1] Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G, Burrows-Hudson S, Messana JM, Levin N, Rajagopalan S, Port FK, Wolfe RA, Saran R. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. *Am J Kidney Dis*. 45(4):658–66, 2005.

[2] Mapes DL, Bragg-Gresham JL, Bommer J, Fukuhara S, McKevitt P, Wikstrom B, Lopes AA. Health-related quality of life in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis*. 2004 Nov;44(5 Suppl 2):54–60

[3] Lowrie EG, Curtin RB, LePain N, Schatell D. Medical outcomes study short form-36: a consistent and powerful predictor of morbidity and mortality in dialysis patients. *Am J Kidney Dis*. 2003 Jun;41(6):1286–92.

[4] Provenzano R, Garcia-Mayol L, Suchinda P, Von Hartitzsch B, Woollen SB, Zabaneh R, Fink JC; POWER Study Group. Once-weekly epoetin alfa for treating the anemia of chronic kidney disease. *Clin Nephrol* 61(6):392–405, 2004.

[5] Lefebvre P, Vekeman F, Sarokhan B, Enny C, Provenzano R, Cremieux PY. Relationship between hemoglobin level and quality of life in anemic patients with chronic kidney disease receiving epoetin alfa. *Curr Med Res Opin*. 22(10):1929–37, 2006.

- **Patients themselves**—through improved social contacts, higher income than disability would pay, and access to benefits that may include an employer group health plan (EGHP)
- **Dialysis providers**—by improving payer mix for dialysis centers
- **Medicare and Social Security**—by reducing the number of ESRD patients who have Medicare as their primary health coverage and the number collecting disability benefits.

More than 354,000 working age patients started dialysis from 1992–2003. Of these, 102,104 were working 6 months prior. More than 71% of these working patients did not receive any EPO to treat their anemia prior to kidney failure, contributing significantly to reduction in employment levels in more than 31,000 patients.[6] In 1973, the Medicare ESRD Program was funded based on the belief that people who received treatment for kidney failure would be active, productive, tax-paying citizens. To the extent that physicians and patients are frightened that appropriate anemia treatment will harm them and patients are undertreated as a result, the goal of keeping patients working will become even more difficult to achieve.

Finally, if there *is* a trade-off to be made between length of life and quality of life (with a lower versus a higher hemoglobin level), *only one person* can legitimately make that choice: *the person with anemia.* I hope the Committee will bear in mind that reimbursement policies ultimately and dramatically affect the day-to-day lives and futures of people with kidney failure.

Perhaps the Committee could consider looking at innovative ways to reduce costs while improving patient outcomes. For example, why not incentivize *patients* to receive their EPO doses subcutaneously, which is more effective and less costly—but requires more needle sticks. Waiving all or a portion of their Medicare Part B premiums ($93.50 monthly in 2007) for patients who accept subcutaneous dosing would likely save considerably more than it would cost. (Incidentally, concerns about pure red cell aplasia with subcutaneous dosing of ESR products in Canada and Europe have now been attributed to the use of uncoated rubber stoppers in the vials, a practice that has now been stopped).[7]

Coalition for Dialysis Patient Choice
December 20, 2006

The Coalition for Dialysis Patient Choice attended the recent Congressional hearing on Patient Safety and Quality Issues in End Stage Renal Disease Treatment and appreciates the opportunity to provide comments to the Committee regarding reimbursement policies for anemia management. The Coalition is a non-profit organization formed by companies and organizations dedicated to increasing the availability of innovative, more physiologic dialysis therapies (more frequent and/or longer duration) and reducing the barriers to home and self-care dialysis.

Given the critical role the Federal government has assumed in the care of dialysis patients, we commend the Committee's efforts to seek optimum care in anemia management. As payment methodologies are revised, our Coalition asks that the potential to increase patient access to home and more frequent dialysis modalities also be considered. Greater utilization of these modalities will assist in addressing the particular anemia management questions raised by this Committee, and also has the potential to lower total Medicare costs and improve beneficiary outcomes.

Hemoglobin levels in the dialysis population and utilization of pharmaceuticals to address anemia are without doubt influenced by payment policy. The same "perverse incentives" that influence in-center IV drug utilization also discourage home therapies. As stated in the Government Accountability Office's (GAO) recent report titled *Bundling Medicare's Payment for Drugs with Payment for All ESRD Services Would Promote Efficiency and Clinical Flexibility,* "Studies have shown that daily hemodialysis—which some experts contend is clinically preferable—reduced the need for Epogen in some ESRD patients with anemia . . . [h]owever, Medicare coverage is limited to three dialysis treatments a week." Evidence supports that home dialysis, whether peritoneal dialysis (PD) or home hemodialysis (HHD), is currently

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[6] Hofmann RM, Schatell D, Witten B, Muehrer R, Gagnon R, Becker BN. Factors contributing to employment of working-age ESRD patients at initiation of dialysis therapy. Publication pending.

[7] Boven K, Knight J, Bader F, Rossert J, Eckardt K, Casadevall N. Epoetin-associated pure red cell aplasia in patients with chronic kidney disease: Solving the mystery. Nephrol Dial Transplant. 20 Suppl 3:iii33–40, 2005.

underutilized—despite the continued evidence reported annually, using Medicare data, that the home setting leads to the lowest total cost of care.

We support the GAO's recommendation for the rapid implementation of the "expanded bundle" as soon as possible. If coupled with appropriate safeguards and case-mix considerations to protect patients from EPO underutilization, this method represents a very effective way to reverse these perverse incentives and their negative unintended consequences. We further favor the implementation of the "expanded bundle" for all beneficiaries as soon as practicable.

However, neither patients nor Medicare will realize the greatest potential benefit if revision in payment policy results only in more efficient utilization of pharmaceuticals within today's most prevalent treatment regimen—thrice weekly hemodialysis in the center, or "conventional" hemodialysis. A large, recent randomized study of conventional dialysis (the NIH/NIDDK's HEMO study) showed that modifications within this treatment regimen were unlikely to lead to significant improvement in patient outcomes. To materially improve patient outcomes and reduce Medicare costs, more significant modifications are required to the way dialysis is delivered. Simply put, significantly better dialysis is required for further improvement, and more frequent/longer dialysis provides this opportunity.

The clinical evidence supporting more frequent and longer dialysis modalities is compelling and growing. By closer approximation of the 24/7 workings of the naturally functioning kidney, more frequent/longer dialysis leads to a number of potential patient benefits. Relevant to this discussion, these therapies have been shown to improve anemia management with lower pharmaceutical needs. In addition, however, these therapies can also:

- Dramatically improve blood pressure management with fewer antihypertensive drug needs
- Better manage patient bone disease and vascular calcification
- Improve patient nutrition
- Improve patient rehabilitation/functional status.

The most natural setting for these therapies is in the home, where the patient retains control of his or her schedule and care. Together, these improvements have the potential to dramatically reduce Medicare ESRD drug and hospitalization expenses currently incurred by conventional dialysis patients (these expenses represent over 60% of the current total annual cost of care), and can facilitate patients' continued contributions as productive members of society.

We believe that the expanded bundle structure, with appropriate performance measures and the implementation of "shared savings" concepts that have been discussed, can be instrumental in encouraging therapies beyond today's conventional, thrice weekly in-center dialysis.

In summary, the Coalition asks that the Committee consider the anemia management questions more broadly, and to take a *total cost of care* perspective when recommending changes. We ask that you explicitly consider the potential to encourage appropriate utilization of home and more frequent/longer dialysis therapies when making payment policy modifications. By doing this, not only will Medicare encourage optimal anemia management but, at the same time, optimize patient care costs and outcomes.

Again, we appreciate the opportunity to provide input into this important process. We stand ready to provide any additional information that will assist the Committee and the community in this valuable work.

Sincerely,

Joseph E. Turk, Jr.
NxStage Medical
Founding Member

Rod Kenley
Aksys Ltd.
Founding Member

Jim Sweeney
Renal Solutions, Inc.
Founding Member

Dori Schatell
Medical Education Institute
Supporting Partner

Statement of Patricia Tate-Harris, Association of Dialysis Advocates, Baton Rouge, Louisiana

The Association of Dialysis Advocates (ADA) is a grassroots patient/family advocacy organization dedicated to ensuring quality, safe care for dialysis patients. ADA is self-funded through personal contributions of our members. We do not accept financial or other contributions from the dialysis industry, pharmaceutical industry, healthcare industry, or any government entity so that we maintain our integrity and objectivity in addressing dialysis-related issues.

ADA is encouraged by the House of Representatives Ways and Means Committee's hearing of December 6, 2006 re: the ESRD Program. We are encouraged that our congressional representatives are holding Centers for Medicare & Medicaid (CMS) accountable for the quality of care provided dialysis patients and for the efficient use of taxpayer dollars that fund care. We are encouraged that our representatives expressed favor towards a "patients come first" policy and pointed to the need for CMS policies to reflect such a policy.

ADA is most grateful for the contributions and support of the Hearing panelists for bringing forth data related to the use of Epogen and its detrimental effect on patients. When this medication is not administered within established guidelines for the benefit of patients, poor patient outcomes can follow. We are also thankful for the recent media interest and coverage that brought information to dialysis patients and taxpayers regarding the clinical and fiscal issues related to use and overuse of Epogen.

The hearing of December 6, 2006 is but another beginning. ADA patients and families are hopeful that the Ways and Means Committee will pursue all issues related to the federal ESRD program so that patients receive quality and safe care at a reasonable cost to taxpayers. ADA has longed believed that attention to the use of Epogen has been a necessity.

ADA's positions regarding specific issues covered during the hearing follow:

EPOGEN

ADA strongly believes that an immediate congressional directive should be given to CMS to incorporate into the federal ESRD Program the recent FDA warning regarding Epogen.

ADA supports bundling of services and drugs, including Epogen. Additionally, ADA supports the clinical individualization of treatment to best meet the needs of the patient. It is essential, ADA believes, that the current financial incentive to overuse Epogen be removed and replaced with emphasis on patient safety. Lastly, ADA believes that the bundling of services and drugs will discourage the overuse of Epogen and focus greater attention upon the adequacy of iron stores—and at lesser cost—for what should be a more efficacious use of Epogen.

ADA supports subcutaneous administration of Epogen. ADA believes that clinical and cost perspectives, as demonstrated by the United States Veterans' Administration Hospitals (as well as in Europe), are supported by subcutaneous administration of Epogen. Further, ADA believes that use of multi-dose vials of Epogen will address existing provider and patient concerns regarding stinging during subcutaneous administration.

Lastly, we request that Congress intervene to ensure that (1) policies, payment and others, are based upon safe delivery of care to patients by experts having no conflict of interest due to their positions, affiliations or relationships within the dialysis industry and/or pharmaceutical companies and that (2) every effort be made to ensure that no one pharmaceutical company monopolizes any medication required for quality treatment of chronic renal failure and/or ESRD patients. This is a population that is escalating—the protection afforded a monopoly is not in the best interest of patients or taxpayers.

INCREASED FUNDING FOR PREVENTION AND SPECIAL INVESTIGATIVE STUDIES

ADA is supportive of the suggestion that NIH be appropriated funding to research the factors that **c** ontribute to over-representation of minorities—particularly African-Americans, Hispanics and Native American Indians—among the kidney failure/dialysis population. We further support a focus upon prevention efforts accompanied by funding that ensures attainment of program goals.

Congress has established 18 ESRD networks to provide quality assurance of the ESRD program. African-Americans comprise 12–13% of the general population yet represents, according to ESRD Networks 2005 Annual Reports, at least 33% of the dialysis population in ten of the eighteen ESRD Network regions. In seven of the ten ESRD Network regions the African-American dialysis population is 40% or greater. Glaringly, the African-American dialysis population in Network 5 (Mary-

land, Virginia, Washington, DC, West Virginia) is 59%; in Network 6 (Georgia, North Carolina, South Carolina) African-Americans comprise 67% of the dialysis population; in Network 8 (Alabama, Mississippi, Tennessee) 62.3%; and Network 13 (Arkansas, Louisiana and Oklahoma) 52.5%. Such over-representation is an event that cannot, and must not, be minimized but rather calls for assertive and aggressive prevention and treatment programs.

CMS' RESPONSIBILITY TO BENEFICIARIES

Among other things, CMS' responsibility to beneficiaries is three-fold: (1) ensuring quality, safe delivery of care (2) ensuring sufficient information is provided in order for beneficiaries to make informed decisions, and (3) ensuring an effective systematicmechanism through which to address patient concerns related to care.

Quality, Safe Delivery of Care

No policy related to quality, safe care is truly meaningful unless it is actually incorporated intothe clinical performance measures and ancillary services required by its respective patient population. All stake-holders from patient-families to healthcare workers fully recognize that it will be incumbent upon Congress to ensure that CMS, ESRD Networks and the state survey agencies each carry out responsibilities related to the oversight and enforcement of ESRD Conditions for Coverage.

The recent exposure of a dialysis facility in Birmingham, Alabama (Birmingham News, November 19, 2006, "*Patients feel they're mistreated: Dialysis centers focus on profits, advocates say*") that had not been inspected since 1998 simply demonstrates the laxity with which CMS, the ESRD Network and state survey agency carried out their statutory, contractual responsibilities. Equally revealing were (1) HHS, Office of Inspector General report, *Availability of Quality of Care Data in the Medicare End Stage Renal Disease Program,* November 2006 report (OEI–05–05–0030) that reflected the ESRD networks' lack of necessary data to identify facilities "with quality improvement needs," and (2) HHS, Office of Inspector General *Civil Monetary Penalty report* (November 2006) that reported a dialysis facility/owner's agreement to pay $150,000 to resolve liability for submission of Medicare claims although ***"inadequate and/or worthless services had been rendered to patients"***—worthless services that the HHS OIG alleged ***"may have contributed to seven deaths . . ."***

Patients' lives are at stake! It is unconscionable that CMS, ESRD networks and state survey agencies have permitted such failures in oversight while dialysis chains/facilities and pharmaceutical companies nevertheless have experienced raging financial returns.

Making Informed Decisions

ADA supports the 2004 ESRD Initiative for Quality Care. However, ADA also firmly believes that the initiative's original intention regarding the Dialysis Facility Compare website and chart was to "empower consumers with quality of care information to make more informed decisions about their healthcare" and such has not been met. Patients and consumers still need "to review and compare facilities and choose a dialysis facility that best meets their needs." While there is information posted regarding anemia, hemodialysis adequacy, and patient survival, ADA believes the information is limited. Dialysis Facility Compare does not provide other highly pertinent information for ordinary patients and/or consumers to truly make informed decisions. For instance, patients and consumers are greatly interested in (a) staffing—including their education, skills knowledge and training, and licensing and/or certification (b) inspection reports, and (c) infections and infection rates. And, most unfortunately, the information provided is not easily understood by ordinary patient-consumers. Both the public disclosure and the simplification of the information found on the Dialysis Facility Compare chart will support informed decision-making while furthering patient education and safety.

CONCLUSION

We, at the Association of Dialysis Advocates, are encouraged and confident that the Ways and Means Committee will be steadfast in its efforts to ensure quality care to dialysis patients and the efficient use of public funds. Similarly, we are encouraged and confident that the Ways and Means Committee will work to ensure that CMS, ESRD Networks, and State Survey Agencies carry forth their responsibilities in the best interest of dialysis patients, their families, and the public. ADA

stands ready to participate and serve in deliberations related to the delivery of care in dialysis environments.

Very truly yours,

Patricia Tate-Harris
President

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